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Sonication Assisted Synthesis of Oligomannosides

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SONICATION ASSISTED SYNTHESIS OF OLIGOMANNOSIDES

by

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in

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ABSTRACT

Sonication-Assisted Synthesis of Oligomannosides

by

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Utah State University, 2009

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Oligomannosides prevalently exist as cell surface antigens. They play important roles in diseases such as viral infection and cancer, and they have been shown to be useful as candidates for vaccines. HIV, one of the most devastating modern diseases, has a high content of mannose sugars on its envelope glycoprotein gp120. Oligomannosides of the HIV virus, also called Man_9, which are found on the glycoprotein gp120, have been shown to play a protective role for the HIV virus, shielding highly conserved protein domains of gp120 from proteolytic attacks. Thus gp120 plays an important role in HIV infection of cells, being responsible for the attachment and penetration of cells to be infected and is thus the target for immunotherapy or vaccine development. The synthesis of complex oligomannosides is still very challenging as numerous methods have been reported but not all are very reproducible.

The use of sonication as a new methodology tool for the synthesis of oligomannosides was investigated. A convenient sonication-mediated protocol applicable

to glycosylation was developed. The synthesis of oligomannosides such as Man_3, Man_6, and Man_9, was achieved under sonication conditions. The use of less reactive or so-called "disarmed" mannopyranosyl donors, such as acyl and thiophenyl donors, was investigated and interestingly the results gave good yields. These disarmed donors are easy to synthesize but it is difficult to perform glycosylation using traditional methods (low yields and longer reaction time). A fast and convenient method for the synthesis of this compound will be very beneficial in this field. Also, the investigation of the solid phase synthesis of carbohydrates under sonication conditions was conducted and the preliminary results were good.

The research investigated a new methodology for the synthesis of complex oligomannosides and oligosaccharides in general and also to improve the glycosylation process where necessary by using sonication methodology and thus establishing an accessible route for the solid phase synthesis of these compounds.

(397 pages)

DEDICATION

I would like to dedicate this work to my dad, Cajetan Maishu Ndze and mum Rosette Beh Ndze, whose blessings have always been with me. My dad wanted me to become a medical doctor which I overheard and wondered how come he is thinking way ahead of time. Unfortunately I couldn't make it to the medical school but I decided to become a doctor anyway not of the medical branch but a doctor of philosophy. I thank you for seeing to it that I have the education I deserve and that I should go all the way wherever my knowledge could take me. I am happy to make you proud on this day and I thank you for being the wonderful and supportive dad that you are. I would like to acknowledge all the support I have received from my sisters and brothers, Teckla, Beri, Liliane, Cajetan, Thierry, and my little nephew Louis. Thank you for your love. Lastly I would like to say thanks to my mum Rosette and dad Cajetan for being the wonderful parents that they are. Their love, patience, and upbringing have made me the person that I am today. Thank you.

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I would also like to thank my family, Brenda Suh, Mathew and Maze Ndonwi, Sylvia Suh for the fun, the talks, and the laughs we have all shared together, not forgetting Mercy Nchang, Gideon Tanifum, and Tchefor and Wano Ndukum. I would like to appreciate the friends I have in my life: Joyce Mumah, Alphonce and Linda Guzha, Yannick Bidias, Marina Fosso, Alvin Lailam, and Relindis and Walters Cheso. Not only have you been wonderful friends but you have also become a part of my family that will never be erased.

To my loving husband Eric A. Tanifum, I wish to say thank you for being a wonderful husband and friend and most importantly a good dad. You made me believe in myself when I couldn't anymore and your support and encouragement have been refreshing. Thank you.

Christabel T. Tanifum

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LIST OF ABBREVIATIONS

Ac: acetyl

Bn: benzyl

Bz: benzoyl

DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene

DMAP: 4-(dimethyl amino)pyridine

DMF: dimethylformamide

NBS: N-bromosuccinimide

NIS: N-iodosuccinimide

Py: pyridine

TBAI: tetrabutylammonium iodide

TEA: triethylamine

Tf: trifluoromethane sulfonate

THF: tetrahydrofuran

TMS: trimethylsilyl

TMSOTf: trimethylsilyl triflate

Trityl: triphenylmethyl

Ts: tosyl

TsOH: *p*-toluenesulfonic acid

TsCl: toluenesulfonyl chloride

LIST OF SPECTRA

Page

CHAPTER I

GENERAL INTRODUCTION

Carbohydrates are ubiquitous in nature and have been found to play fundamental roles in biological systems encompassing cell proliferation, immune response, cell adhesion and cell-cell recognition.[1] Carbohydrates are a major source of energy and they are prime biological substances, of which tons and tons are produced every year through the process of photosynthesis by plants and microorganisms. They constitute the major components of shells of insects, crabs and lobsters, and the supporting tissue of plants. They are also present as parts of all cell walls, spanning the world of microbes to mammals.[2] They occur in various forms from simple sugars to polysaccharides or as conjugates to other biomolecules such as proteoglycans. Carbohydrates were long neglected by drug development researchers due to the underestimation of their biological potential, but scientific evolvement has shown that these molecules have significant diagnostic and therapeutic potential. There exist a great relationship between carbohydrate structure and many biological functions due to their diversity and complexity.

The resurgence of interest in carbohydrate chemistry is due to the fact that carbohydrates have been shown to be a major source of drug leads.[3] It is now believed that carbohydrates may provide the missing clues to the puzzling questions: why are there unusual properties of the Human Immunodeficiency Virus (HIV) and why is AIDS so difficult to treat. Furthermore, how does bacteria, viruses and toxins evade the immune system and initiate infective processes, as well as why are some tumor cells able to

migrate from their original cancerous sites. As scientists develop new antibiotics or modify natural antibiotics towards bacteria defense, bacteria at the same time developed constantly growing resistance against various antibiotics. A classical example of these can be seen with the aminoglycosides class of antibiotics. These compounds, including neomycin B, streptomycin, kanamycin B, and pyranmycin (figure 1), are highly potent broad spectrum antibiotics, but their effectiveness is now being hampered by the emergence of bacterial strains that are resistant to these drugs.[4]

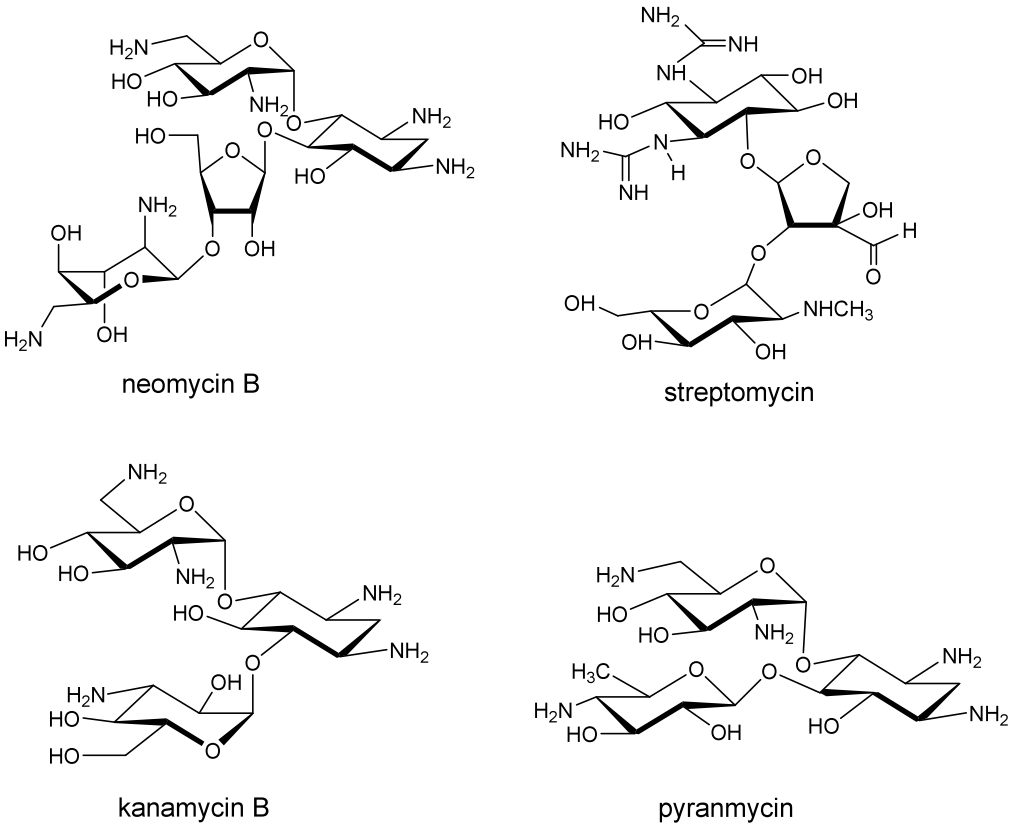


Figure 1: Broad spectrum antibiotic aminoglycosides

The functional specialization and diversity of biologically active carbohydrate molecules and their role in diseases are now well understood. Different types of unique carbohydrate-containing biomolecules are found on all cell surfaces. Many carbohydrates are information carriers and recognition molecules due to their unique structural diversity. Studies have shown that carbohydrates provide signals for protein targeting and serve as binding receptors for toxins, viruses, and hormones.[5] They also control vital events in fertilization and early development.[6] They regulate several critical immune system recognition events,[7] and target aging cells for destruction.[5] Cell-cell interactions such as antigen-antibody or virus-host interactions are some examples of the aforementioned biochemical functions.

I.1 Classification

Carbohydrates occur as monomers (glucose, mannose, fructose), dimers (sucrose, lactose), oligomers or polymers (starch, cellulose), or as components of biopolymers (RNA, DNA) and other naturally occurring biomolecules. The monomers exist as aldoses, which are polyhydroxyaldehydes (figure 2), and ketoses, polyhydroxyketones (figure 3). Aldoses and ketoses can be of different chain lengths and are all derived from glyceraldehyde and dihydroxyacetone respectively (figure 4). Glyceraldehyde occurs in two main enantiomeric forms, which are (+)-D-glyceraldehyde with the (*R*)-configuration and (-)-L-glyceraldehyde with (*S*)-configuration (figure 4). For monosaccharides with more than one chiral center, the D- or L- notation is derived from the configuration of chiral center furthest from the carbonyl. If the configuration is (*R*)-, it is termed a D-sugar and if (*S*)-, it is an L-sugar. Our main focus will be on the D-sugars as they are the most

common in living organisms. Monosaccharides with more than six carbon atoms are relatively rare.

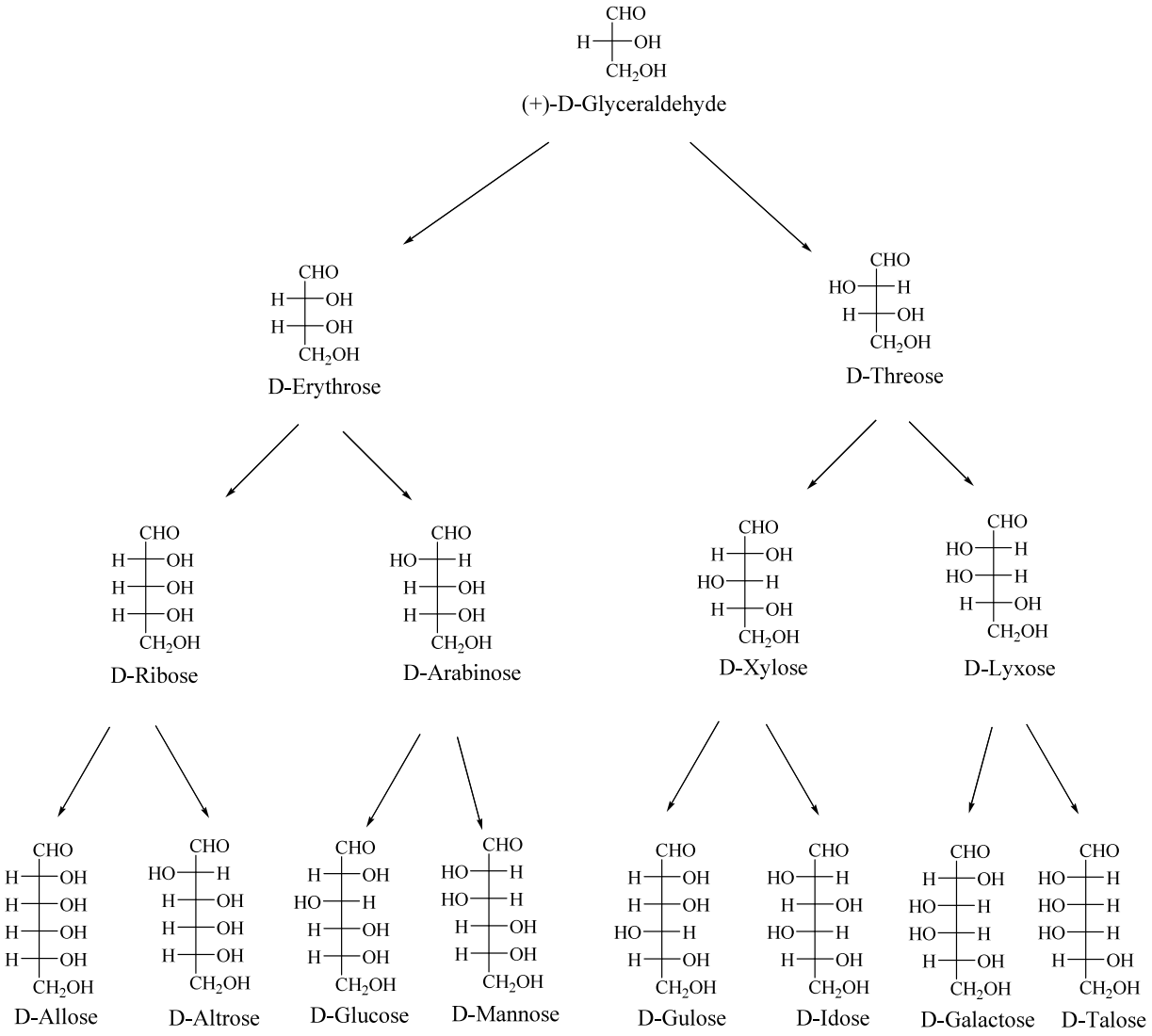


Figure 2: The acyclic forms of D-aldoses

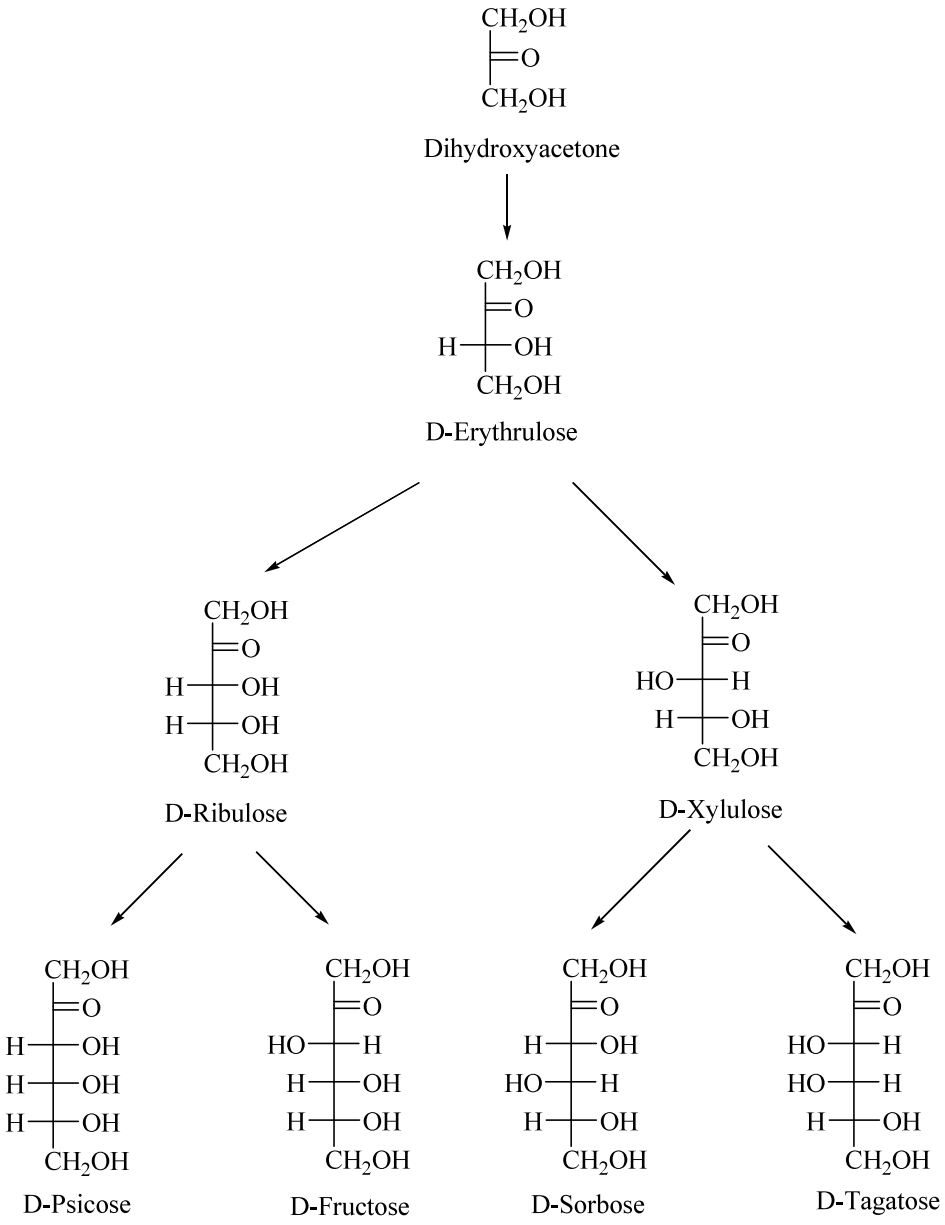


Figure 3: The acyclic form of D-ketoses

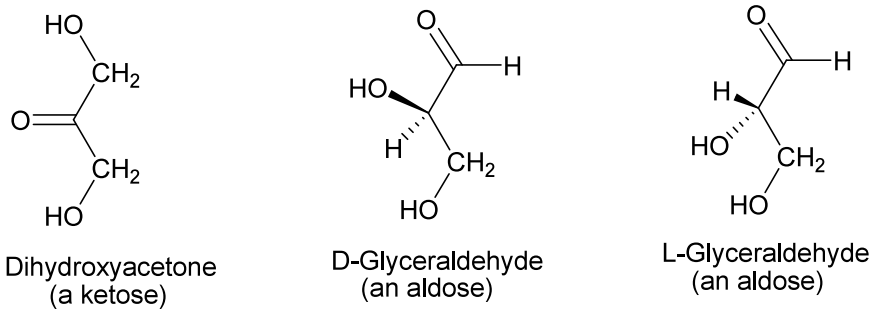


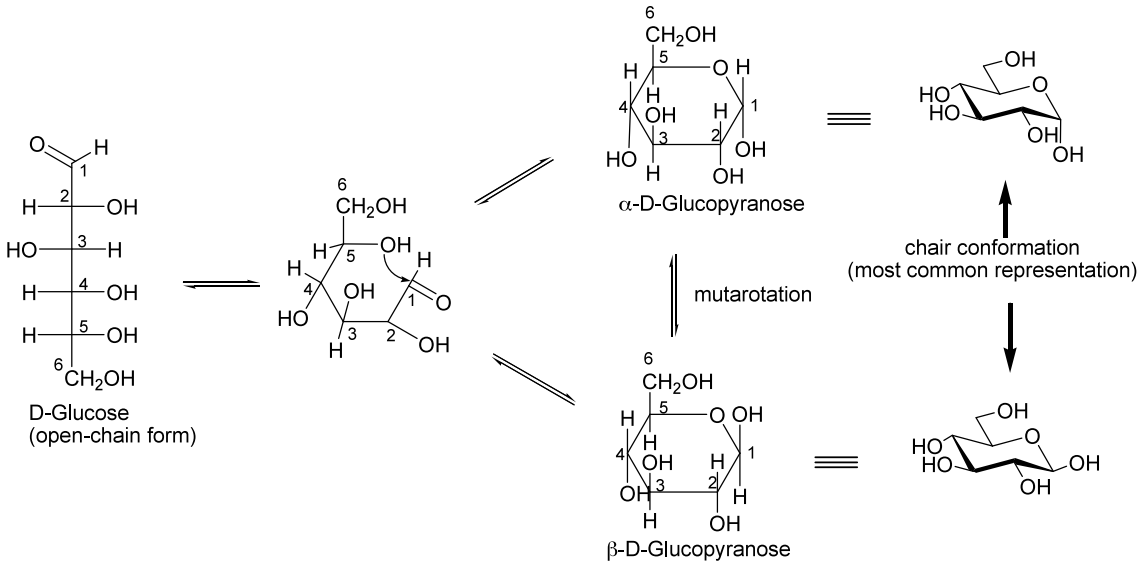
Figure 4: Structure of ketose and aldoses

Monosaccharides can be found in open chain and in ring forms. They exist preferably as cyclic hemiacetals and hemiketals, which arise from the intramolecular nucleophilic attack of a hydroxyl-oxygen atom at the carbonyl atom (scheme 1). Depending on which hydroxyl group reacts, five or six membered rings are formed which are called furanoses and pyranoses respectively. The ensuing hemiacetal hydroxyl group from the reaction could either be in axial position, in which case the product is referred to as the α-anomer or in equatorial position, in which case it is referred to as the β-anomer.

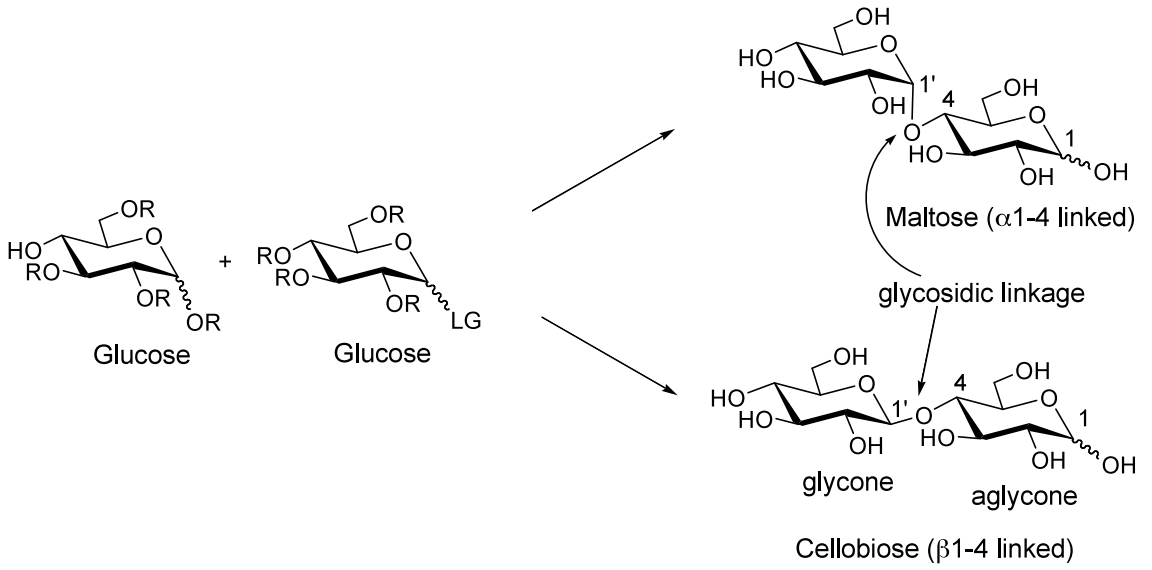
For the graphic representation of monosaccharide structures, several different descriptions are used such as Fisher projection, zigzag projection, Mills projection, Haworth projection, and the chair conformation. Fisher and zigzag projections are only used for acyclic structures. Cyclic sugars are represented by the Mills projection, especially when they are part of other larger structures which are non-carbohydrate rings (as example we have macrolides). The 6-membered ring of monosaccharides is not planar but adopts a regular chair conformation. Thus the cyclic forms of carbohydrates are most accurately drawn as chairs. This representation also facilitates the distinction between the

axial and equatorial positions, a difference which is very important in carbohydrate chemistry.

The monosaccharides are the simplest monomer building blocks. Condensation of two of these monomers by a reaction termed glycosylation (scheme 2) yields a disaccharide such as maltose and cellobiose. The remaining free hydroxyl groups can be further glycosylated to higher linear or branched oligosaccharides and polysaccharides. Disaccharide units are often found as component of many polysaccharides compounds. Disaccharides, which are the simplest oligosaccharides, can also be easily obtained by the hydrolysis of abundant polysaccharides. For example, maltose is obtained from starch while sucrose is extracted from sugar cane.



Scheme 1: Formation of the two cyclic forms of D-glucose



Scheme 2: Glycosylation

Oligosaccharides and polysaccharides are often found as components of proteins and lipids in all cell walls mediating a variety of events such as inflammation, cell-cell recognition, immunological response, metastasis, and fertilization.[8] Each cell type displays different carbohydrates at its cell surface and these are often used as chemical markers. Specific carbohydrates have been identified as markers for certain types of tumors[9] while others are binding sites for bacterial and viral pathogens.[10]

Polysaccharides, also called glycans, differ from each other in the identity of their recurring monosaccharide units, in the length of their chains, in the types of bonds linking the units, and in the degree of branching. There are two types of polysaccharides (figure 5): the homopolysaccharides which contain a single type of monomer and can serve as storage forms used as fuels (example: starch, glycogen) while others serve as structural elements in plant cell walls and animal exoskeletons (example cellulose and chitin).

The heteropolysaccharides, on the other hand, provide extracellular support for organisms of all kingdoms (example peptidoglycan found on bacteria cell walls). Some polysaccharides serve as destination labels for some proteins and as mediators of specific cell-cell interactions and interactions between cells and the extracellular matrix. The informational carbohydrates covalently joined to a protein or a lipid, form a complex called glycoconjugates, which are the biologically active molecules.

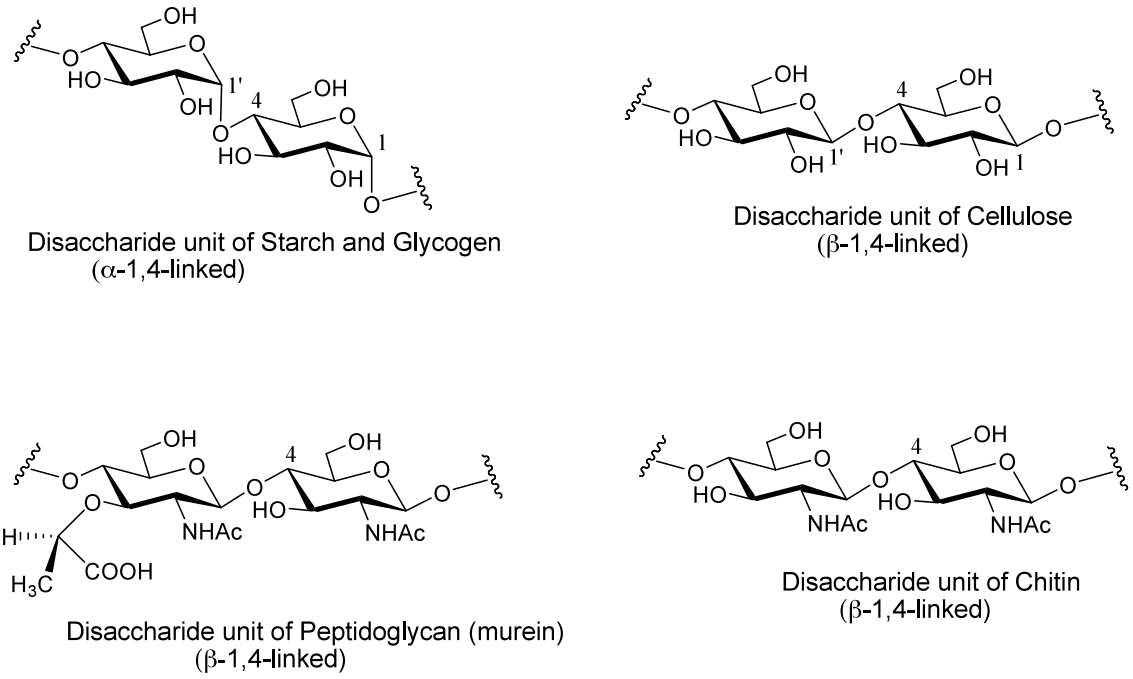


Figure 5: Disaccharide unit of some polysaccharides

I.1.1 Carbohydrate drugs

Many drugs contain carbohydrate moieties as part of their structures. In some cases, removal of the sugar moiety eliminates the therapeutic value of the drug. Due to the multifunctionality of carbohydrates, it is useful to classify biologically active carbohydrates according to their therapeutic activity[5] such as anticonvulsant, anti-inflammatory, anticancer, antidiabetic, antibiotic, and antiviral (figure 6). On the other hand, traditional classification would divide the existing drugs or new analogs into the following classes of derivatives: mono- and disaccharides, oligosaccharides, and polysaccharides.

As an anticonvulsant agent,[11] topiramate is an effective anti-epileptic drug in late-phase clinical trials. The antidiabetic agent MDL 73945,[12] is an inhibitor of intestinal α-glucohydrolases and is under the evaluation for treatment of non-insulin dependent diabetes mellitus. Acarbose,[13] an α-glucosidase inhibitor, is effective in the treatment of patients whose non-insulin dependent diabetes mellitus cannot be managed by diet alone. The antitumor agent, 3-deoxy-3-fluoro-phosphatidyl inositol, for example, inhibits cancer cell growth by inhibiting the signaling pathways, and mediates the effect of activated oncogenes.[14] Cell surface carbohydrates are known to change upon malignant transformation,[15] and are more responsible for the differences in surface properties between metastatic and nonmestatic cells.[16] The antibiotic agents Everninomycins[17] are active against a variety of strains of *Staphylococcus*, *Streptococcus*, *Bacillus* and *Mycobacteria*. The antiviral agent 4-guanidino-NEU5Ac2en[18] inhibits the replication of both influenza A and B viruses in cell culture and is effective in animal models when

administered intranasally. The anti-inflammatory agent sialyl Lewis X, is a blood group antigen.[19] Sialyl Lewis is a tetrasaccharide of glycolipids, which is displayed on the surface of white blood cells and is responsible for the repair of injured tissues.

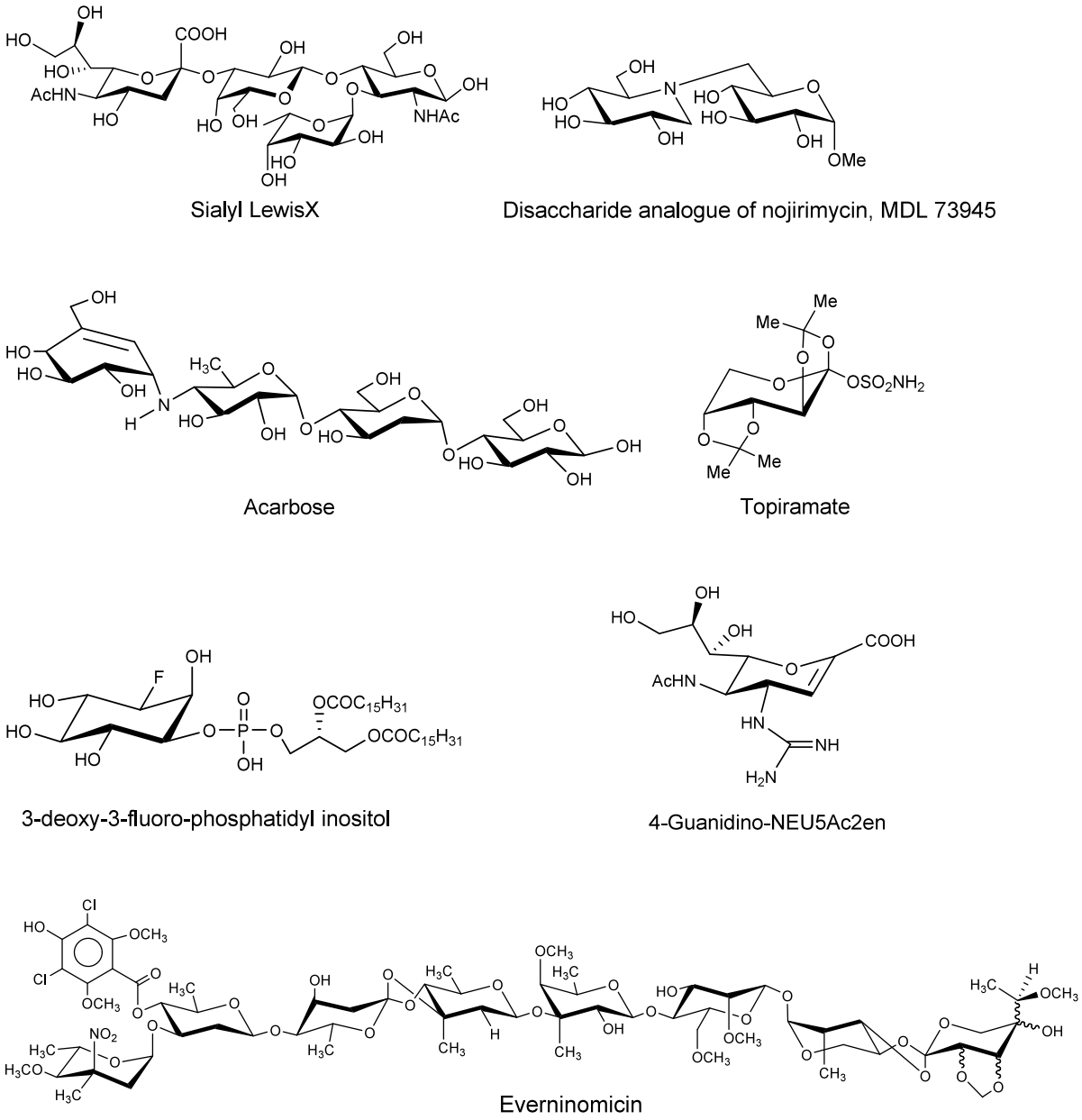


Figure 6: Some carbohydrates with biological potential

I.1.2 Glycoconjugates

As mentioned above, oligosaccharides and polysaccharides are often found attached to proteins and lipids (figure 7). This produces a large number of glycoconjugates, called glycoproteins, proteoglycans, glycolipids, and GPI anchors, respectively.[20] Proteoglycans are macromolecules of the cell surface or extracellular matrix in which one or more polysaccharide chains, also called glycosaminoglycan chains, are joined covalently to a membrane protein. They have a polyanionic character and consist mainly of repeating disaccharide subunits, which are often *O*-sulfated. They are major components of connective tissue, such as cartilage. Glycolipids are membrane lipids in which the hydrophilic head groups have oligosaccharides which act as specific sites for recognition by carbohydrate-binding proteins.

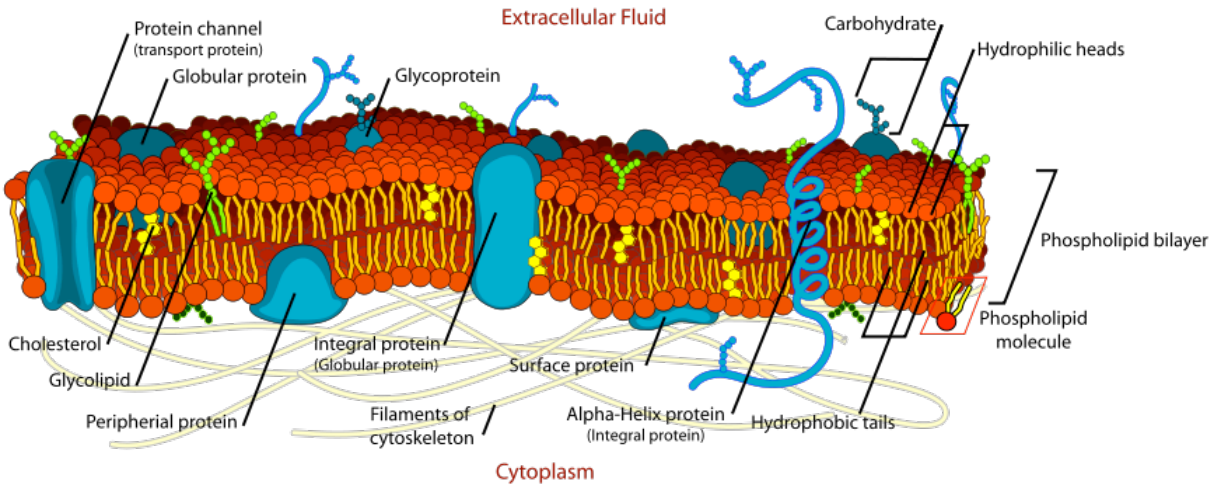
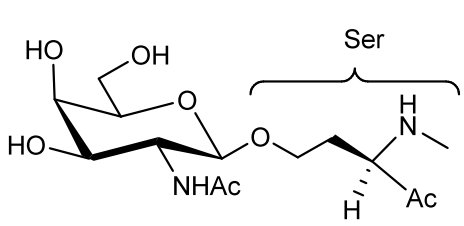


Figure 7: Glycoproteins and glycolipids[21]

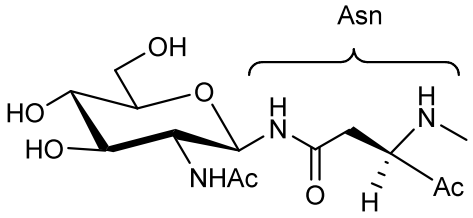
Glycoproteins are carbohydrate conjugates in which the carbohydrate moieties are smaller and more structurally diverse than the glycosaminoglycans of proteoglycans. Glycoproteins are more rich in information than glycosaminoglycans. There are three important type of linkages by which carbohydrates are covalently bound to proteins (figure 8). The first type of glycoprotein linkage is the *O*-glycans which usually contain an *N*-acetylgalactosamine attached through a glycosidic bond to the *O*-terminus of either threonine or serine. The second form of *O*-linked glycan consists of a galactose or a glucosyl-galactose disaccharide linked to the hydroxyl group of hydroxylysine. *O*-linked glycoproteins assemble their oligosaccharides on the polypeptide chain.

The second type of glycoprotein linkage is the *N*-linked glycans, which involve a glycosidic bond between *N*-acetylglucosamine and the N-terminus of an asparagine residue.[22] The third type of linkage, involves attachment through ethanolamine phosphate, which occurs in glycosylphosphatidylinositols called GPI anchors. In contrast with the *O*-linked glycoprotiens, *N*-linked glycoproteins assemble their oligosaccharide portions on a lipid linked intermediate, dolichol phosphate.

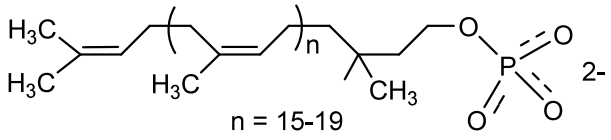
Glycophorin A (figure 9), for example, is a glycoprotein that spans the plasma membrane ("Lipid bilayer") of human red blood cells.[23] As shown on the figure, fifteen carbohydrate chains are *O*-linked to serine and threonine and one carbohydrate chain is linked to the asparagine (at position 26). Glycophorin A is the most important attachment site by which the parasite *Plasmodium falciparum* invades human red blood cells.



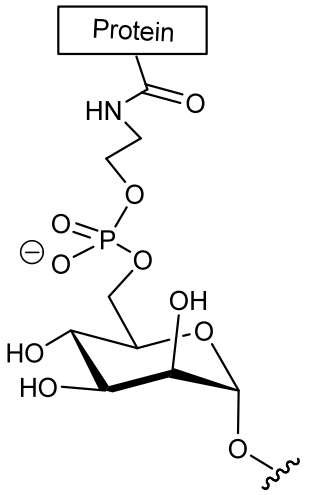
O-linked GalNAc



N-linked GlcNAc



Dolichol Phosphate



Via ethanolamine phosphate

Figure 8: The different types of glycoprotein linkages

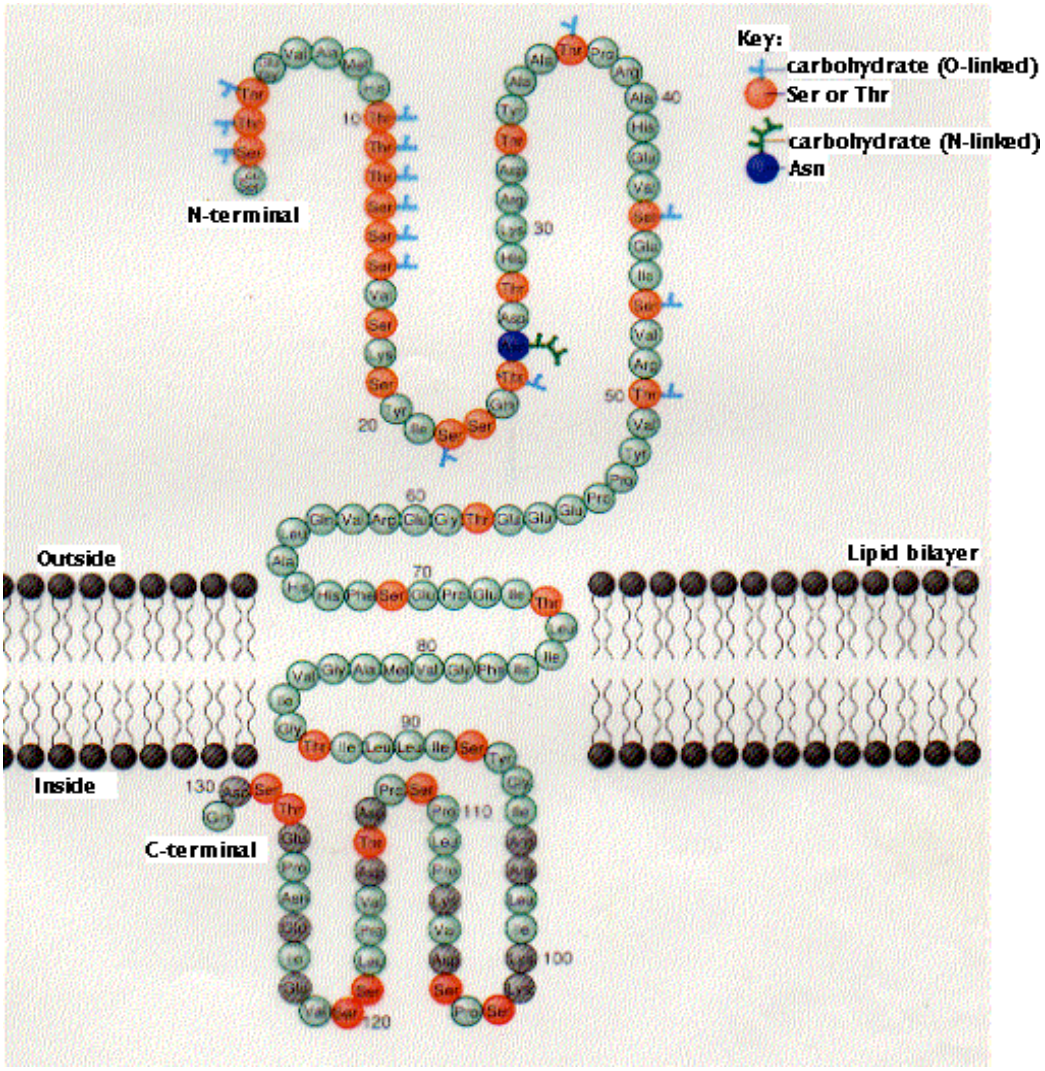


Figure 9: Structure of glycophorin A[24]

Most glycoproteins share a peptide-linked pentasaccharide fragment called the core region which consist of Man-(α1,6)[Man-(α1,3)]Man-(β1,4)-GlcNAc-(β1,4)-GlcNAc (figure 10), with the terminal GlcNAc *N*-glycosidically linked to an asparagine residue of the peptide chain.[25] Attached to this uniform core region, are oligosaccharide chains with different saccharides leading to branched or unbranched structures. Based on this finding, *N*-glycans have been classified into three types: The high mannose-type, the complex-type, and the hybrid-type.

The simplest *N*-glycans are high mannose-type oligosaccharides (also called oligomannosides) which contain only α-mannosyl residues bound to the branching *N*-glycoprotein core. In complex type, the α-mannose residues forming the bisecting core are elongated with *N*-acetylglucosamine residues and *N*-acetyllactosamine (Galβ1-4GlcNAc) disaccharide moieties.

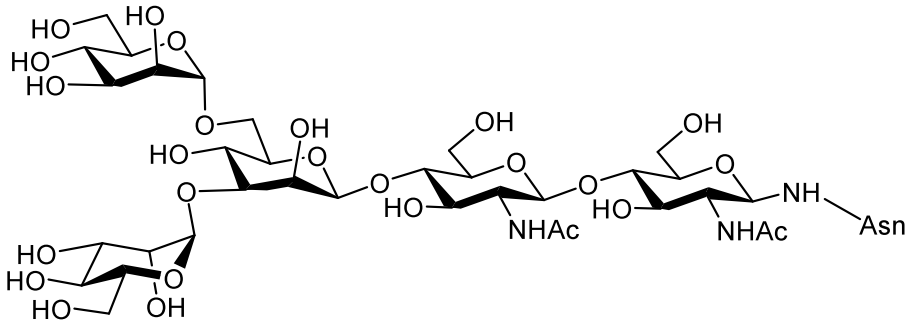


Figure 10: Structure of Man-(α1,6)[Man-(α1,3)]Man-(β1,4)-GlcNAc-(β1,4)-GlcNAc

Oligomannosides are ubiquitous in nature and have been found to be involved in important biological functions. This explains why many scientists are interested in their synthesis (more detailed discussion on this later). The oligosaccharide portions of glycoproteins are rich in information. They form highly specific sites for recognition and high-affinity binding by other proteins. They function as molecular addresses and by interaction with specific receptors, they can orchestrate a variety of biological functions in intercellular communication, such as cell proliferation, cell-cell adhesion, and cell migration. Molecules which can decode the information stored in carbohydrates are called lectins. These are proteins, which are specialized for the specific recognition of carbohydrate ligands resulting in the formation of non-covalent carbohydrate-protein (lectin) complexes.

I.2 Lectins

Lectins, non-enzymatic sugar-binding proteins, play an important role in biological recognition phenomena involving cells and proteins.[26] They possess unique structural features which provide them the ability to discriminate among a gamut of complex carbohydrate structures found on the surface of cells, invading microorganisms, in intracellular matrices, as well as those attached to soluble glycoproteins. Although first discovered in plants and microorganisms, lectins are now known to be widely distributed in animals as well.[27] The discussion in this section will be focused on animal lectins.

Lectins have the ability to selectively bind with free sugars as well as sugar residues of polysaccharides, glycoproteins, and glycolipids. Surfactant protein D (SP-D) for example shows monosaccharide specificity in the order maltose>glucose>mannose.[28]

Lectins bind monosaccharides rather weakly, but employ the same strategies for enhanced affinity and specificity in binding more complex oligomers.[29] X-ray crystallography studies reveal that relatively low affinity binding sites for monosaccharides are formed at shallow indentations on protein surfaces, while selectivity is achieved by a combination of hydrogen bonding to the sugar hydroxyl groups and van der Waals packing. This often includes packing of a hydrophobic sugar face against aromatic amino acid side chains. Higher selectivity is achieved through additional direct and water-mediated contact between oligosaccharides and the protein surface. The higher affinity for oligomers results from clustering of simple binding sites in oligomers of the lectin, while the geometry of such oligomers helps to establish the selectivity.[30]

Several animal lectins can selectively bind to the surface of intruding bacterial and viral pathogens and initiate steps towards their neutralization. Others mediate adhesion between animal cells, sorting of newly synthesized glycoproteins in the endoplasmic recticulum, and endocytosis of selected subsets of circulating glycoproteins.[30]

Animal lectins are classified based on the nature of their carbohydrate ligands, the biological activity, subcellular localization, and divalent cation dependence.[27] The carbohydrate-binding section of lectins, known as the carbohydrate-recognition domain (CRD) are generally conserved within each subclass of lectins. CRDs within a major class may be further subdivided based on properties different from structural similarities. Animal lectins consist of three groups, (i) the S-type lectins, (ii) the C-type lectins, and (iii) the P-type lectins. S-type lectins do not require any divalent ions for their activity,

but require reducing agents (thiols) for full activity. They are intra- and extracellular, and specifically bind β-galactosides.[27] Among the P-type lectins, the most prominent example is the mannose-6-phosphate receptor, which serves as targeting of glycosylated lysosomal enzymes to their subcellular compartments.

On the other hand, lectins with CRDs which require calcium ions for their activity for example, are designated C-type lectins. They are also extracellular and bind a variety of sugars. C-type lectins are comprised of endocytic lectins, collectins, and selectins (L-, E-, P-selectin).

One of the most prominent representatives of the C-type lectin is the mannose-binding protein (MBP) expressed on macrophages; these are important cells of the immune system which engulf and destroy infectious organisms after receptor binding. This type of defense not depending on antibodies is called innate immunity. Another group is the mannose-binding proteins which are soluble lectins present in mammalian serum and liver. They bind to oligomannosides on infectious microorganisms, causing activation of compliment without antibody participation, and subsequent lysis of the pathogens.

Mannose-binding lectin is a calcium-dependent serum protein that plays a role in the innate immune response by binding to carbohydrates on the surface of a wide range of pathogens (viruses, bacteria, fungi, protozoa), where it can activate the complement system or act directly as an opsonin.[31] The complement system is a set of plasma proteins that work together to attack extracelluar pathogens. While the most important role of the complement system is to opsonize pathogens (by making them more liable to destruction

by phagocytes), it also recruits inflammatory cells and kills pathogens directly through membrane attack complexes. Once MBP recognizes a pathogen, its lectin domain will bind to mannose, or other carbohydrate sugar residues on the pathogen surface, and activate complement via the MB-lectin pathway. Many lectins occur as oligomers such as MBP which occurs as a trimer (figure 11).

Different lectins specific for the same oligosaccharide may recognize different regions on its surface. Due to the flexibility of oligosaccharides (freedom of rotation around the glycosidic bonds), the selection of a specific three-dimensional oligosaccharide structure from the array of existing structures is one of the most important features of lectin-sugar interactions which awaits elucidation.

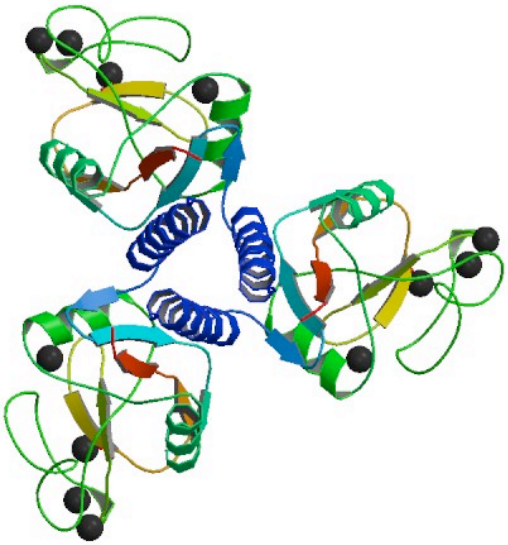


Figure 11: Representation of mannose-binding protein[32] (MBP trimer)

Man_9, which is the oligomannoside found on the gp120 glycoprotein envelope of the human immunodeficiency virus (HIV), is one of the most important oligosaccharides that have attracted many researchers due to their role in the HIV infection.

I.3 Oligomannosides and their role with HIV

Oligomannosides are oligosaccharides that consist of only mannose as the monomer. Mannose is absorbed eight times slower than glucose. When digested, mannose goes directly from the upper gastrointestinal (GI) tract to the blood stream instead of being converted into glycogen, or stored in the liver. Of the eight essential sugars for optimal health in humans, mannose is the most important. It is involved in more cell actions than any other essential sugars and deficiencies in mannose can lead to a whole host of physical problems.

Mannose is essential in communication between cells and also in the inhibition of tumor growth and spread and the prevention of parasitic, bacterial, viral, and fungal infections. It is necessary for the production of cytokines which fight infections and diseases. It has been found to also ease inflammation from rheumatoid arthritis, lower blood sugar and triglyceride levels in diabetics, and also help in urinary tract infections.

Figure 12 below shows the bacterium *Escherichia coli* adhering to the cells lining the bladder and urinary tract through the fimbria on their cell walls.[33] The fimbria contains glycoproteins that bind to the first molecule of sugar that it encounters, which is mannose in this case. Mannose is found on the surfaces of these cells and act as receptors, inviting the fimbria of *E. coli* to attach and allowing them to bind tightly to the tissue. When mannose is ingested, it goes directly to the urinary system and binds competitively

to the bacterial lectins, occupying sites that would normally bind host cell mannose receptors, which prevents attachment; without attachment, infection is prevented.

Oligomannosides are important in cell–cell communication involved in both normal functions and diseases and as receptors on cell surface; they are an important part of disease processes such as cancer and inflammation. They are found in nature as essential substructures of many bioactive glycoconjugates such as *N*-glycans, fungal cell wall mannans,[34] and glycosylphosphatidylinositol molecules (GPI anchors).[35] They also occur as high affinity ligands for mannose 6-phosphate receptors.[36]

Figure 12: *Escherichia coli* adhering to human intestinal cells[33]

HIV, one of the most devastating modern diseases, has a high content of mannose sugars on its envelope. HIV infection occurs via virus-cell and cell-cell fusions mediated by the two envelope glycoproteins, gp120 and gp41[37-39] (figure 13). In fact gp120 plays an important role in the HIV infection of cells, being responsible for the attachment and penetration of cells to be infected. For this reason, it is a target for immunotherapy or vaccine development. Gp120 binds to CD4 and chemokine receptors, triggering a series of events that lead to the insertion of the fusion peptide of gp41 into the target membrane and subsequent membrane fusion.[40] This leads to a conformational change of gp41 causing it to snap shut into a six helix coiled-coil bundle. The surface of gp120 is characterized by an abundance of high mannose *N*-linked glycosylation sites.

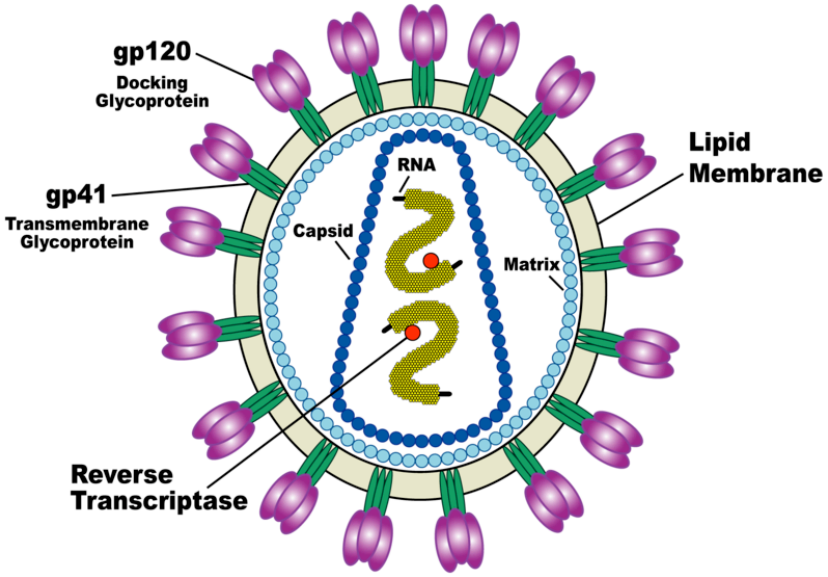


Figure 13: Structure of HIV viron[41]

Post-translational glycosylation of gp120 covers conserved portions of the protein with host generated carbohydrates that constitute almost half of the molecular mass of gp120 and limit recognition by the immune system, thereby allowing HIV to evade detection and destruction.

Few antibodies have been isolated which successfully bind to the immunologically silent region of gp120 which is the heavily glycosylated exposed face. The carbohydrates moieties found on the envelope glycoprotein gp120 of the HIV virus, are promising targets for immunogen design as demonstrated by a potent neutralizing human monoclonal antibody 2G12. 2G12 (an antibody that binds to a portion of the silent region of gp120) is capable of neutralizing a broad range of HIV strains.[42] A successful vaccine approach would seek to elicit a focused immune response of 2G12-like antibodies by exposing the immune system to an effective-scanning mimic of the 2G12 epitope. The dense carbohydrate coat on the HIV-1 envelope provides a strong defense for the virus to evade humoral immune recognition. However, this strong shield is not completely seamless. HIV-1 surface carbohydrates have proven to be targets for developing anti-HIV strategy (as example there is cyanovirin-N and some lectins specific for oligomannose structures which have demonstrated anti-HIV activities in *in-vitro* assays).[43]

Besides this relationship between oligomannoses and HIV, branched oligomannoses are also integral structural components of asparagine-linked glycans (*N*-glycan), one of the major types of postsynthetic protein modifications.[1] *N*-glycans are involved in many fundamental biological processes such as cell differentiation, viral

infection, nascent protein processing and tumor migration.[44] The neutralizing antibody 2G12[45] and the anti-HIV protein cyanovirin-N specifically target high mannose sugars on the surface of gp120[46,47] (figure 14). Cyanovirin is a cyanobacterial protein isolated from *Nostoc ellipsosprum*,[48] that inhibits HIV-1 fusion at nanomolar concentrations through tight binding to the high mannose type oligosaccharides (Man_9 and Man_8) of gp120.

Another cyanobacterial protein, MVL isolated from a laboratory culture of *Microcystis viridis* NIES-102,[50] has been shown to inhibit HIV-1 envelope-mediated cell fusion at nanomolar concentrations by binding to high-mannose *N*-linked carbohydrates, Man_9 (figure 15), on the surface of the envelope glycoprotein gp120.[51] Cyanovirin and MVL are unusual in that they bind oligosaccharides with very high affinity in the absence of multivalent interactions. Cyanovirin-N specifically recognizes the disaccharide Manα(1-2)Manα (in blue) located at the terminal branches of mammalian high mannose oligosaccharides.[45,47,52] In contrast, MVL is specific to its target which is the Manα(1-6)Manβ(1-4)GlcNAcβ(1-4)GlcNAc tetrasaccharide core (in red) found in *N*-linked oligomannosides.[51]

The existence of broadly neutralizing antibody 2G12, and the characterization of its epitope as a novel oligosaccharide cluster on HIV-1 gp120, raises a possibility of developing a carbohydrate-based vaccine against HIV-AIDS. However, carbohydrate antigens have not been adequately exploited for HIV-1 vaccine design, despite their abundance on HIV-1 surface.[53] The exploration of various HIV-1 glycopeptides as new and unique epitopes, may open a new avenue for vaccine development. Efficient

syntheses of branched oligomannoses can therefore provide much needed materials to facilitate their biological studies.

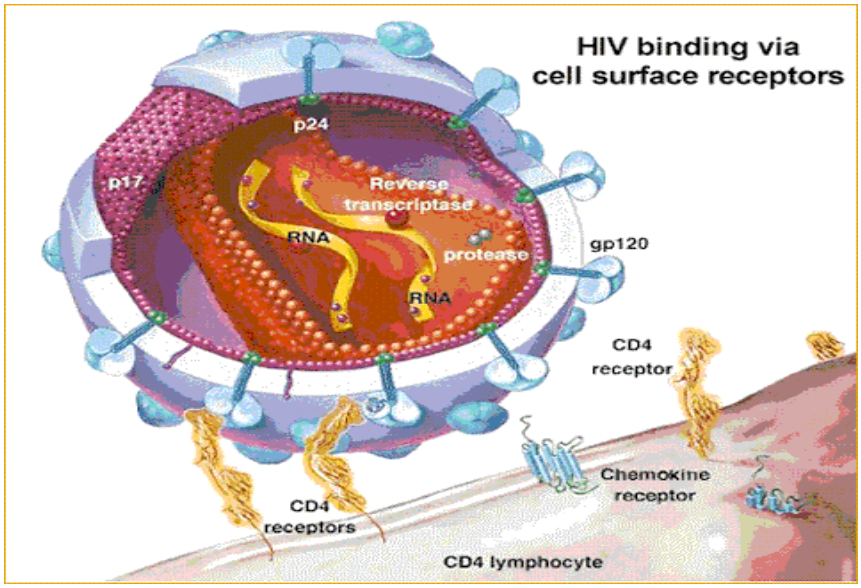


Figure 14: Carbohydrates in cell-cell recognition[49] (CV-N blocks the gp120-CD4 fusion)

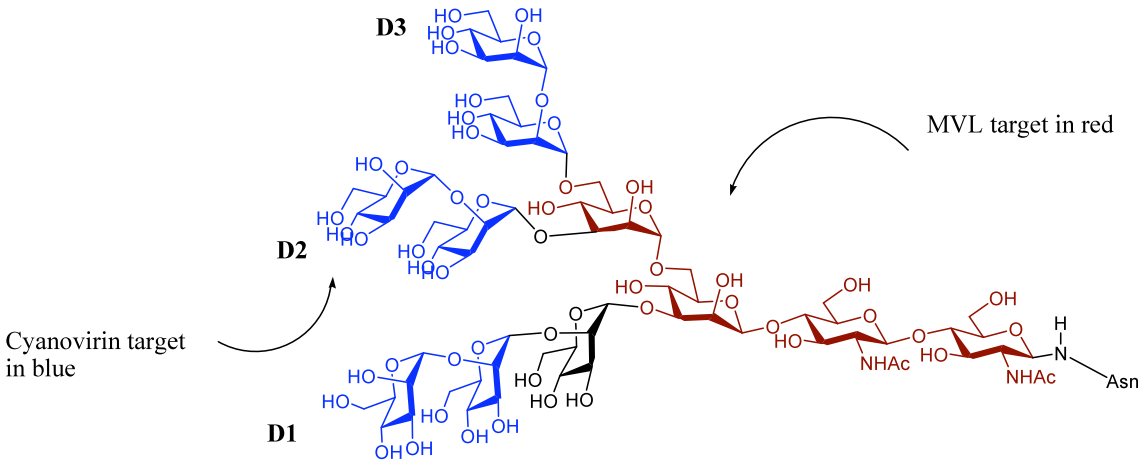


Figure 15: Structure of $Man_9GlcNAc_2$

I.4 Synthetic Methods

Currently, the synthesis of oligosaccharides is being pursued by researchers from different areas.[54-57] Carbohydrate synthesis is achieved through a process called glycosylation protocol. This implies the activation of a suitable glycosyl donor equipped with a leaving group at the anomeric center and the efficient and stereoselective coupling to a glycosyl acceptor, which is promoted by a suitable activator. Several synthetic methods for activating various glycosyl donors have been developed.[53,58,59] Sophisticated methods, such as one-pot programmable glycosylation,[60,61] chemoenzymatic synthesis,[62] solid-phase oligosaccharide synthesis,[63,64] and iterative glycosylation,[65] have been developed with the aim of alleviating the challenges faced in oligosaccharides synthesis. However, the diverse and complicated methods found in the literature[57,63,66] do not always make it easy for researchers to select the best approach to synthesize the desired oligosaccharides. This is due to the fact that different carbohydrate (glycosyl donors or acceptors), manifest moderate to drastic reactivity depending on the reaction conditions. And sometimes, optimization of the reaction conditions for each carbohydrate moiety is very problematic. Moreover, few of these methods are reproducible or yield enough material to use for biological studies.

There are still two types of glycosylation where the efficiency is not always satisfactory. The first type is the case where large glycosyl donors are used in a reaction and the second type is when glycosylation is carried out at multiple sites simultaneaously. For example, solid-phase oligosaccharide synthesis often requires excess glycosyl donors (5 – 10 equiv.) to achieve the desired outcome. Also very complex to expensive reagents

have been used to achieve glycosylation and these are seldom used in the synthesis of oligosaccharides.

As mentioned above, one of the key factors in oligosaccharide synthesis is the reactivity and the stability of the leaving group (glycosyl donor) and the conditions used to activate one over the other. Glycosyl donors (figure 16), such as glycosyl halides,[67] glycosyl trichloroacetimidate,[68] thioglycosyl donors,[69] O-acyl donor,[70] *n*-pentenyl glycoside,[71] glycosyl sulfoxide,[72] have all been developed and used in carbohydrate synthesis, but not all have been efficient in the synthesis of oligosaccharides.

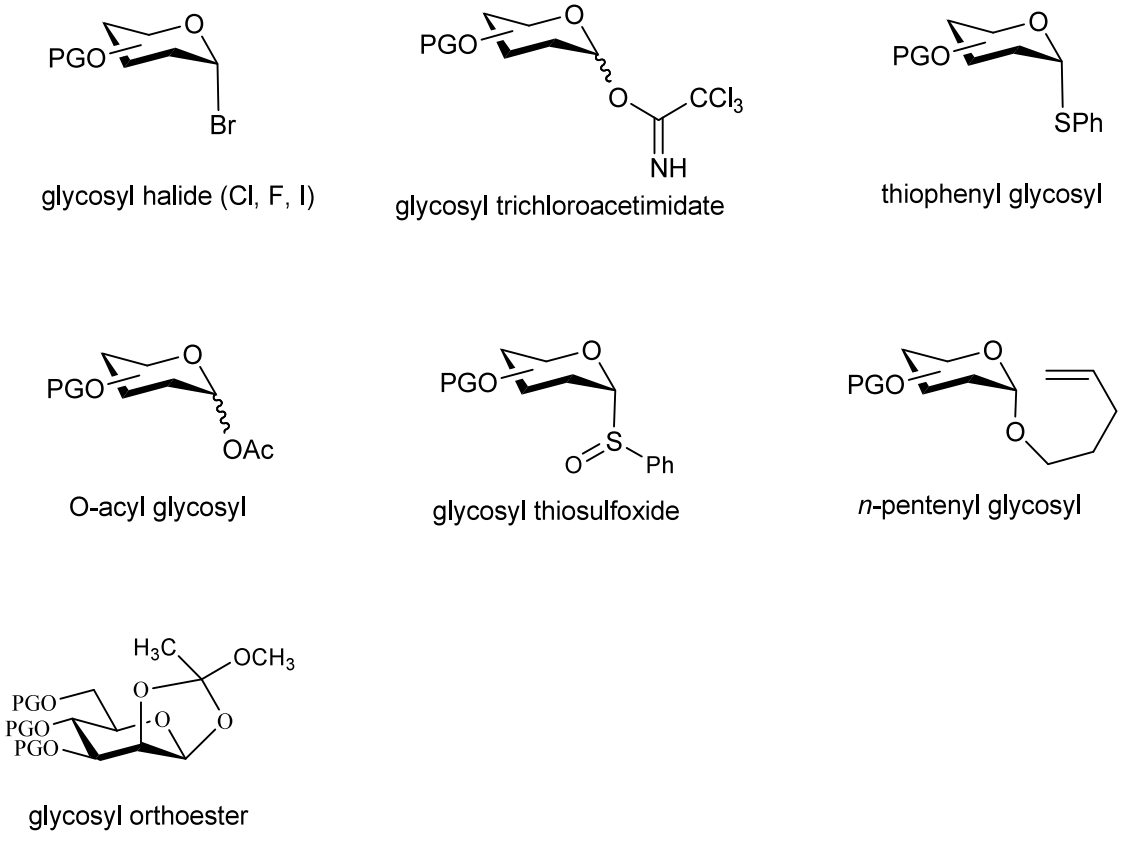


Figure 16: The different glycosyl donors

In this regard, the development of new synthetic methodologies, which can provide adequate protocols with cheaper starting materials are much needed. In an attempt to further contribute to the synthetic methods that are currently in use, our attention was focused on the synthesis of oligomannosides under sonication methodology. Sonication,[73-77] also called sonochemistry, has long been employed as the energy source for enhancing the rate of chemical reactions. It has been employed in many traditional chemical reactions as it provides the needed energy to overcome the different reactivity among various carbohydrate derivatives. It may enable the development of general protocols for facilitating the synthesis of complex carbohydrates.

Our research group has been able to synthesize carbohydrate compounds with the use of sonication for various glycosylations.[78] Sonication has proven to be time efficient and the yields obtained have been very encouraging. The use of sonication for sterically hindered compounds has also proven to be successful in our laboratory. Our emphasis will be on the study of glycosylations using mannose-based donors, such as phenylthiomannosides and mannosyl acetate donors. These donors are known for their relatively low reactivity as compared to the other glycosyl donors, such as glycosyl trichloroacetimidate and glycosyl halide. Glycosylation reactions carried out under sonication conditions have been accomplished in a matter of minutes and the yields have been very good. This methodology was then applied into the synthesis of complex oligomannoside Man_9,[79,80] which has been shown to have immense therapeutic applications.[81] Although the synthesis of Man_9 has been accomplished, the lengthened

synthetic steps and the reaction time are not very encouraging if one intends to repeat it's synthetic schemes.

The aim of this research was to investigate the use of sonication as a new methodology tool for the synthesis of complex oligomannosides such as Man_9. Before the synthesis of Man_9 could be attempted, simpler molecules had to be synthesized using sonication before attemting the synthesis of more complex carbohydrates. Stereoselectivity in glycosylation using mannose sugar very often favors the α-anomer and the synthesis of β-mannosides is often very problematic. Experiments were carried out under the same condition with different solvents to attempt to yield a better stereoselectivity. This was then followed by the synthesis of monosaccharides using a single acceptor: 6-azidohexanol. This choice was based on the fact that, the azide group could be reduced to an amine group which will then facilitate the attachment of the sugar to a carrier protein to enable some biological testing. The synthesis of disaccharides and trisaccharides was then achieved, followed by the synthesis of more complex oligomannosides Man_6 and Man_9. Solid phase synthesis under sonication was also investigated as it could be a means of shortening the synthetic steps involved in solution phase synthesis, which often require multiple purification steps.

CHAPTER II

SOLUTION PHASE SYNTHESIS OF OLIGOMANNOSIDES

Oligomannosides possess a variety of important biological implications and applications such as regulating immune response,[82] mediating cellular interactions,[83] utilized as tumor-associated antigens,[81] involved in fungal infection,[84] viral[85] and bacterial[86] pathogens. As a result, the synthesis of structurally diverse natural and non-natural oligomannosides as potential therapeutic agents has been pursued by various researchers.[87] Some strategies for the conventional step-wise solution phase synthesis of oligosaccharides have been developed. These involve selective protection, followed by glycosylation and deprotection sequences which are time consuming and require chromatographic purification of all intermediates. In addition, while these work well for glucose and galactose sugars, they do not work well for mannose. So the search for new and expedient methods for oligosaccharide synthesis is imperative. Indeed, several research groups across the globe are currently pursuing research in this area.

To contribute to this effort, sonication was investigated as a new method for the expedient synthesis of oligomannosides. As stated earlier, sonication has been employed to enhance the rate of many traditional chemical reactions[73-77] including carbohydrate chemistry.[88] However, only a few examples of glycosylation reactions employing glycosyl donors such as unprotected donors,[89] glycosyl halides,[90] and glycosyl sulfones[91] have been reported. In this investigation, efforts were directed towards the development of general protocols of glycosylation using mannose-based donors including phenylthiomannosides and mannose acetate. These two donors are relatively stable and

can be prepared in large quantities. Their reactivity is low compared to glycosyl trichloroacetimidate and glycosyl halide, especially in the presence of acyl protecting groups.

II.1 Sonication or Sonochemistry

The study of ultrasonic chemical effect is a research area that is expanding rapidly. The most recent applications of sonochemistry are in the synthesis and modification of both organic and inorganic chemistry.[92] In 1927, two researchers Alfred Lee Loomis and Robert Williams were the first to report the effect of ultrasonic waves in liquid media.[93] Sonochemistry was rejuvenated in the 80s when inexpensive reliable instruments with high intensity ultrasound, were made available. Ultrasound wave often produces very high temperatures (5000 K) and pressures, and increases chemical reactivity by up to a million fold.[94] In the laboratory, ultrasound is applied using an ultrasonic bath or probe known as sonicator. It has many applications which include degassing liquids, deactivating biological materials, cleaning instruments or extracting microfossils from rocks.[94]

In chemistry, energy is one of the most important things that chemical reactions need in order to occur. Energy derived from ultrasound differs greatly from that generated from traditional sources (such as heat, light, ionization) in the duration, the pressure and the energy per molecule.[95] Ultrasonic waves have a unique means of driving chemical reactions under extreme conditions.[96] Unlike sonochemical reactions, traditional reactions involve a direct interaction between the molecular species and its surrounding such as bond breaking. The mechanism of sonochemistry is dependent upon two major factors which are: the intensification of mass-transfer processes and acoustic cavitation.[97]

Cavitation is defined as the formation of bubbles, followed by the growth and then the implosive collapse of these bubbles. This yields an enormous rise of local temperatures and pressures.

The role of cavitation is that it concentrates the diffuse energy of sound. When cavitation causes bubble collapse, this generates intense localized hot spots, high pressures and very short life times. These extreme conditions can cause chemical bond to rupture. It should be noted that cavitation in a homogenous liquid system is quite different from that of a liquid solid system. Cavities grow rapidly and reach sizes where they can efficiently absorb energy generated by the sound field and when overgrown, they can no longer absorb the sound energy and implode.[95]

The chemical enhancement of reactions by ultrasound has beneficial applications in mixed phase synthesis, material chemistry, and in biomedical uses. In chemical kinetics for example, it has been observed that ultrasound can greatly enhance chemical reactivity in a number of systems, effectively acting as catalyst by exciting the atomic and molecular modes of the system.[98] When gas compresses, heat is generated in irradiated liquid, compression of cavities increases collapse of bubble. This generates a short-lived localized hot spot which is the source of homogeneous sonochemistry.

In this chapter, we present our findings on the influence of sonication on the synthesis of oligomannosides. The results obtained show that glycosylation reactions carried out under sonication proceed much faster and with better yields than those carried out under traditional conditions. There is also some evidence that with the right solvent choice, sonication also leads to superior selectivity between α and β anomers. Also, glycosylation carried out on secondary alcohols only afforded α anomers. Some concepts

in the stereoselectivity of glycosylation are first discussed followed by the first part of this research which covers the synthesis of glycosyl donors and acceptors (acetyl and thiophenyl-based), which are the starting materials for glycosylation reactions. This is then followed by the exploration of solvent effects on stereoselectivity and yields, and glycoslation test runs using some of the donors with 6-azidohexanol as the acceptor. These provided some knowledge on the stereoselectivity of mannose-based compounds and the desired solvents in which to run the glycosylation reactions after which, the synthesis of dimannosides, trimannosides, and more complex oligomannosides including Man_9 was achieved.

Glycosylation which is the condensation of two molecules, one being a glycone moiety (donor) and the other an aglycon often occurs at the anomeric center. Glycosylation is a key step in the synthesis of oligosaccharides in general. Oligomannoside synthesis is achieve through glycosylation methodology necessitating the activation of a donor with a leaving group at the anomeric center and the stereoselective coupling to an acceptor, promoted by a good activator to lead to the desired compound. The stereochemical outcome of glycosylation could depend on whether or not the substituent at C-2 is participating in the mechanism of the reaction.

II.2 General concepts on stereoselectivity in glycosylation reactions

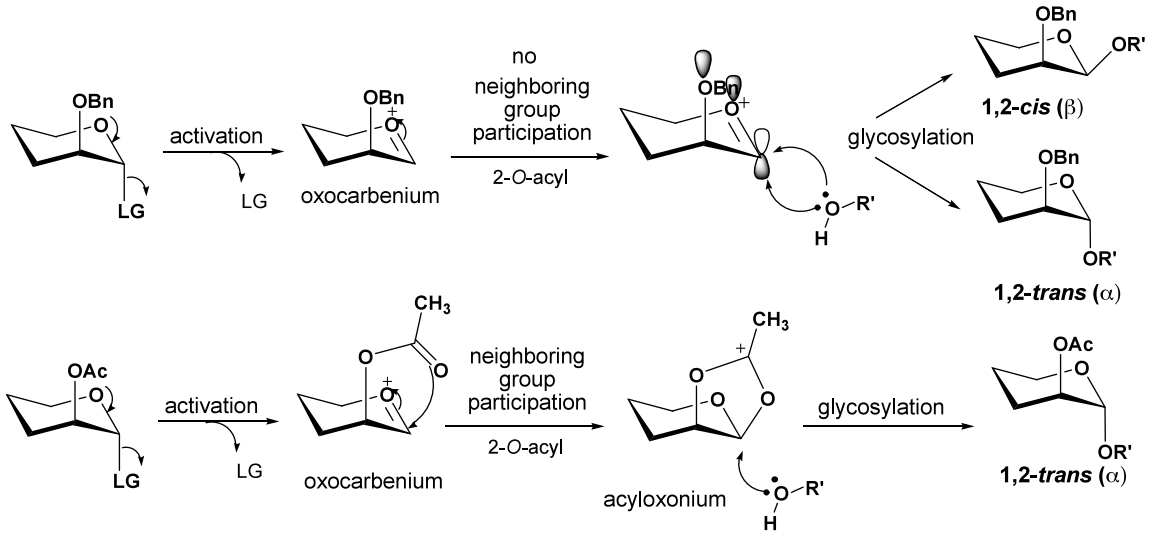
II.2.1 Neighboring group participation

During a glycosylation reaction, there is the formation of an oxocarbenium intermediate which is formed. The participation of the substituent at C-2 (such as ester groups), would lead to the formation of an acyloxonium intermediate which can react with a nucleophile in the opposite direction (or trans-cleavage), yielding the 1,2-trans

glycoside (scheme 3). In the case of mannose sugar with the axial orientation at C-2, the formation of the acyloxonium is greatly enhanced due to the reverse anomeric effect.[2] Benzoate or pivaloate groups at C-2 are less favored to form the acyloxonium intermediate compare to acetate group. Also ether groups at C-2 will not favor any 1,2-orthoester intermediate.

II.2.2 Anomeric effect

Generally, substituents at the equatorial position of a sugar ring are thermodynamically favored over those at the axial position when they adopt their chair conformation. For D-pyranoses and compounds with electronegative groups at the anomeric center, the α-derivatives at the axial position are often more stable than it has been predicted by steric hindrance with neighboring substituents.[2]



Scheme 3: Mechanism depicting the neighboring group effect

During the anomeric effect, a lone pair of electrons located in the n-molecular orbital of atom Y (or O) overlaps with the antibonding σ*-orbital of the C-X bond leading to a favorable delocalization of nonbonding electrons (figure 17). This is only possible with an anti-periplanar arrangement of the involved orbitals. Also, the anomeric effect is strongly influenced by the nature of the substituent at C-2 as it is proportional to the electronegativity of the atom at C-1, and it is greatly enhanced in the case of mannose which has an axial C-2-substituent. The nature of the anomeric group is important for anomeric effect as it depends on the electronegativity of the substituent bound at this center. Solvents also influence the anomeric effect. More polar solvents decrease the influence of the anomeric effect on the equilibration of α and β conformers in solution.[2]

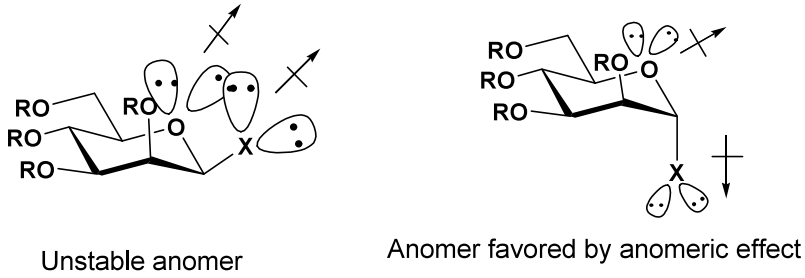
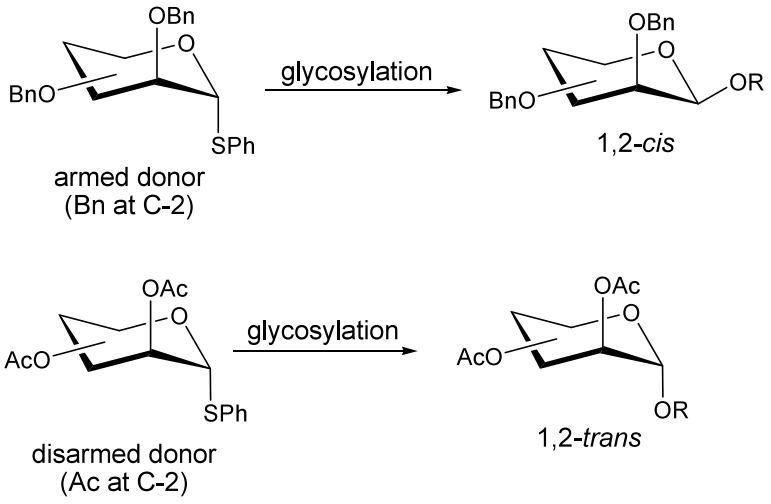


Figure 17: Stable and unstable anomers

II.2.3 Armed and disarmed concept

The reactivity of the anomeric center depends on the sugar and mostly on the substituents. The reactivities of the different glycosyl donors can also be used to explain the stereochemistry of the products. In the late 1970s, Paulsen's group observed that electron withdrawing groups such as acyl groups reduce the reactivity at the anomeric center leading to the term "disarmed glycosyl donor," while electron donating groups such as benzyl ethers, enhance the reactivity and are classified as "armed glycosyl donors." Also the reactivity may depend on the nature of substituent at C-2 (scheme 4).



Scheme 4: Concept of stereoselective glycosylation

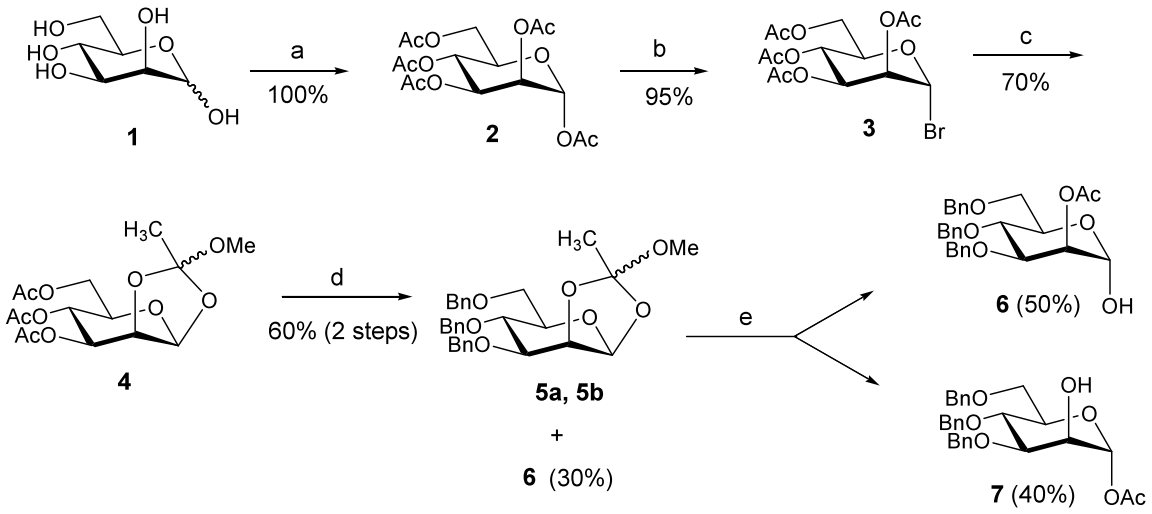
II.3 Synthesis of mannose-based monosaccharide derivatives

The synthesis of donor **5**[99] (scheme 5) started with the acetylation of the commercially available α-D-mannose **1,** to give a mannose pentaacetate **2**. Compound **2** was then treated with a mixture of hydrobromic and acetic acids to selectively brominate the anomeric acetyl group to give **3**. Treatment of **3** with silver oxide in anhydrous methanol and toluene gave the orthoester **4**. Methanolysis of **4** followed by benzylation gave the orthoester donor **5** and a byproduct **6** obtained from the workup (1N hydrochloric acid solution). It should be noted that during workup, if the reaction mixture is not washed with 1N hydrochloric acid, little to no byproduct **6,** is obtained. When **5** was diluted with CH_2Cl_2, mixed with 1N HCl and stirred for 2 hrs, **6** and **7** were obtained.

Compound **6** could be transformed into 2 major donors **8**[100] and **9**. First the acetylation of compound **6** using triethylamine as the base gave acetyl donor **8**. Also, **6** could be transformed to the more reactive trichloroacetimidate donor **9** using trichloroacetonitrile and a catalytic amount of DBU (scheme 6). Though donor **9** is very reactive, it also decomposes very fast during glycosylation. So it is not always a very good donor to use and reactions with this donor are not always 100% effective.

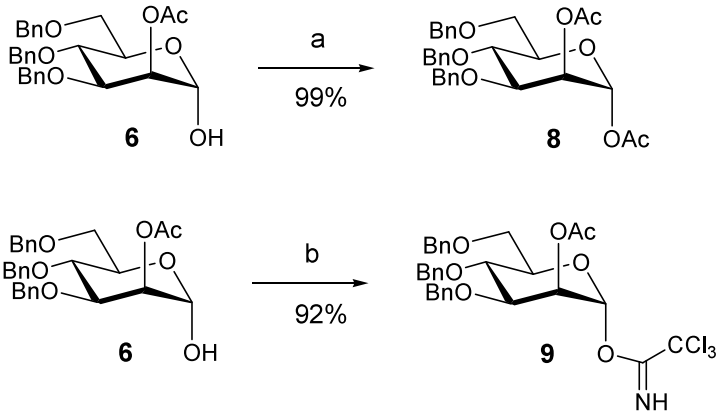
The treatment of the orthoester **5** with thiophenol in acidic medium using sonication, gave glycosyl donor **10**[99] and another product **11**[101] (scheme 7). Under reflux conditions, this reaction usually takes 3 to 5 hours to complete, but under sonication conditions, the reaction is complete within 10 to 30 minutes depending on the quantity of starting material used (1 to 5 g). The yield is also very good compared to traditional methods. The formation of **11** is also greatly reduced under sonication. Methanolysis of

the acetyl group of each of these compounds, **10** and **11,** gave the glycosyl acceptors **12**[102] and **13**[101], respectively.



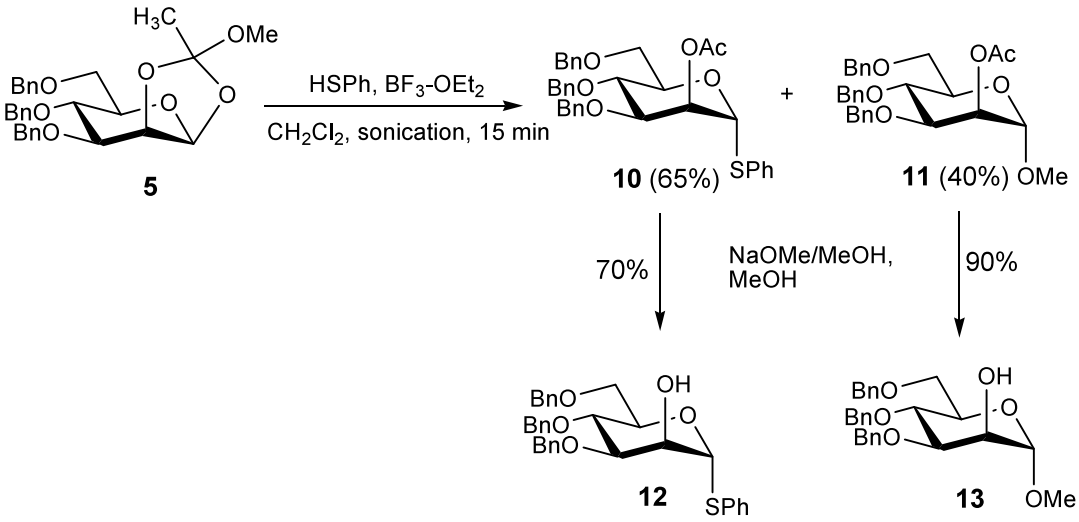
(a) Ac_2O, AcOH, H_2SO_4, 0 ^oC, 1 hr; (b) HBr / AcOH, CH_2Cl_2, 0 ^oC, 5 hr; (c), MeOH, Ag_2O, Toluene, 1 hr; (d) i) NaOMe / MeOH, MeOH, 1 hr, ii) BnBr, NaH, DMF; (e) CH_2Cl_2, 1N, HCl, 2 hr

Scheme 5: Synthesis of D-mannopyranose donor **5**



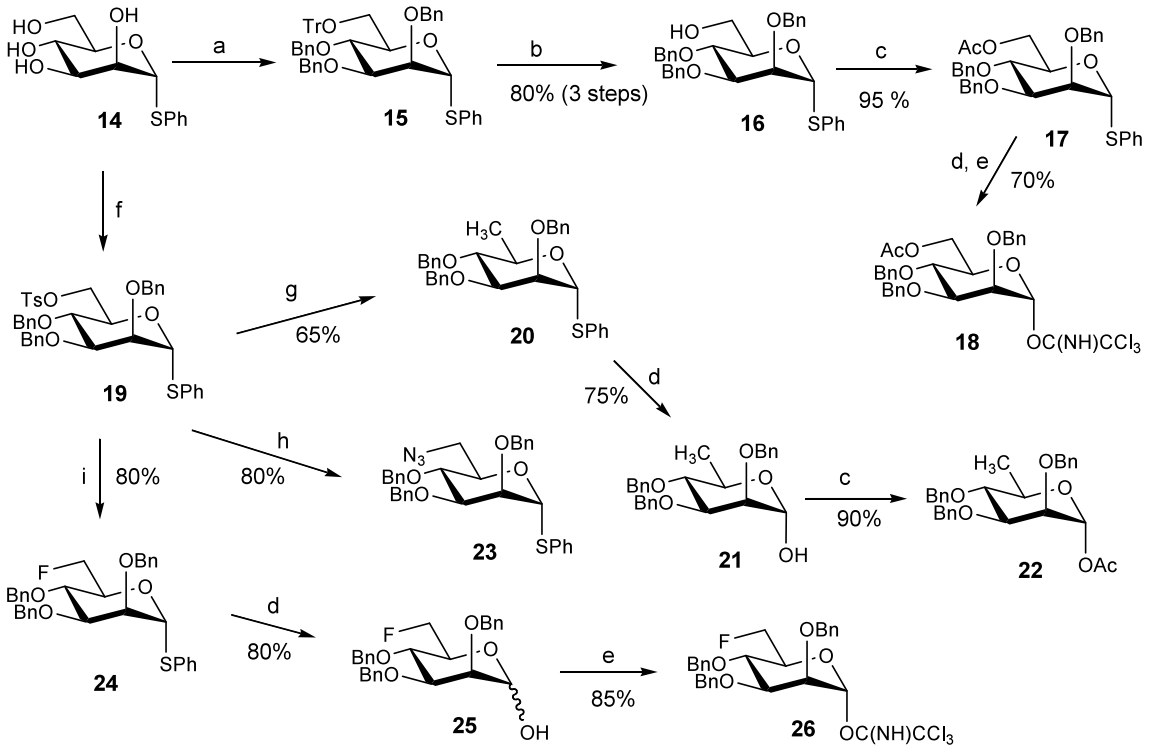
(a) Ac_2O, TEA, DMAP, CH_2Cl_2, 1 hr; (b) CCl_3CN, DBU, CH_2Cl_2, 1 hr

Scheme 6: Synthesis of donors **8** and **9**



Scheme 7: Synthesis of D-mannopyranose donor and acceptor

The synthesis of mannose derivatives (scheme 8) began with the selective protection of the primary alcohol in **14** using trityl chloride in basic medium, followed by benzylation of the remaining hydroxyl groups to give **15**. Deprotection of the primary alcohol in **15** using a mild acid gave acceptor **16**. Acetylation of **16** gave donor **17,**[103] which was treated with NBS to yield 1-OH intermediate that was further treated with trichloroacetonitrile and DBU to give trichloroacetimidate donor **18**. Again, the hydroxyl group at position 6 of compound **14** was selectively activated using tosyl chloride, followed by benzylation to give **19**. Reduction of **19** using lithium aluminum hydride, gave donor **20** which was further treated with NBS to give **21** followed by acetylation to give **22**. Azido substitution of the tosyl group in **19** gave **23**, while treatment of **19** with TBAF in acetonitrile under reflux gave **24**. Treatment of **24** with NBS gave **25**, followed by acetylation to give **26**. The synthesis of these donors was carried out to enable the synthesis of Man_9 analogs, upon development of a successful methodology.

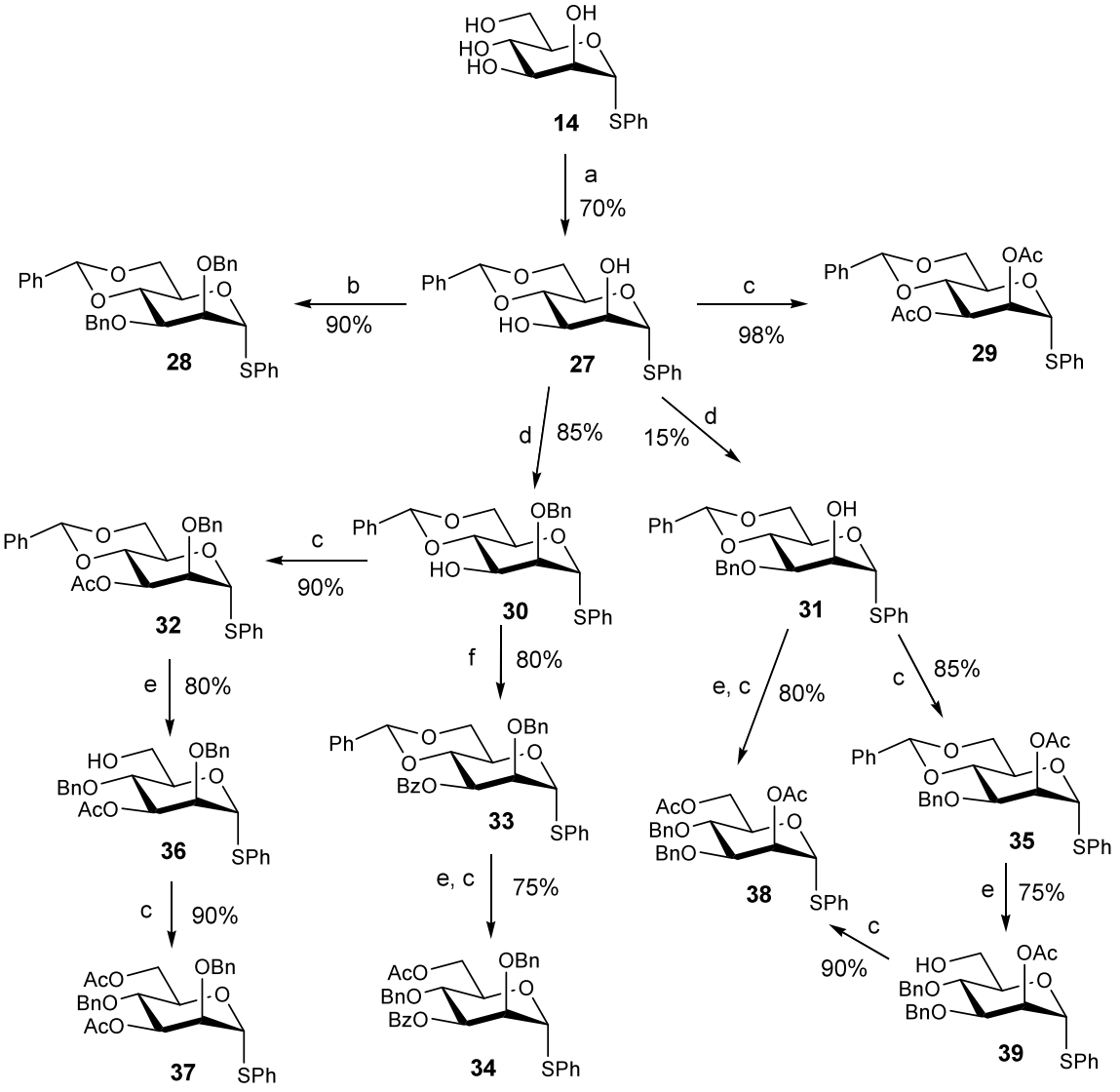


(a) (1) TrCl, TEA, DMAP, CH_2Cl_2, (2) BnBr, NaH, DMF, TBAI; (b) $TsOH.H_2O$, CH_2Cl_2, MeOH; (c) Ac_2O, TEA, DMAP, CH_2Cl_2; (d) NBS, acetone, H_2O; (e) CCl_3CN, DBU, CH_2Cl_2, 15 min; (f) (1) TsCl, pyridine, (2) BnBr, NaH, DMF, TBAI; (g) $LiAlH_4$, THF; (h) NaN_3, DMF, 80 ^oC; (i) TBAF, CH_3CN, reflux

Scheme 8: Synthesis α-D-mannopyranose derivatives

As shown in scheme 9, compound **14** was used to generate many other donors. The 4- and 6- positions were first selectively protected using benzylidene acetal. This gave compound **27,** which was subjected to different types of reactions. First, it was benzylated to give donor **28**[104] and also acetylated to give donor **29**. Selective benzylation using tetrabutylammonium hydrogen sulfate as the key reagent gave compounds **30** and **31**. Compound **30** was acetylated to give donor **32**[105] which was further subjected to a selective deprotection of the benzylidene group to give **36**. Acetylation of **36** gave donor **37**.[106] Compound **30** again was treated with benzoyl chloride to give **33**. The selective

deprotection of the benzylidene group on **33** followed by acetylation gave donor **34**. On the other hand, selective deprotection of **31** followed by acetylation gave **38**. On the other hand, direct acetylation of **31** gave donor **35**. Treatment of **35** with borane tetrahydrofuran complex gave **39** which was then acetylated to give **38**.

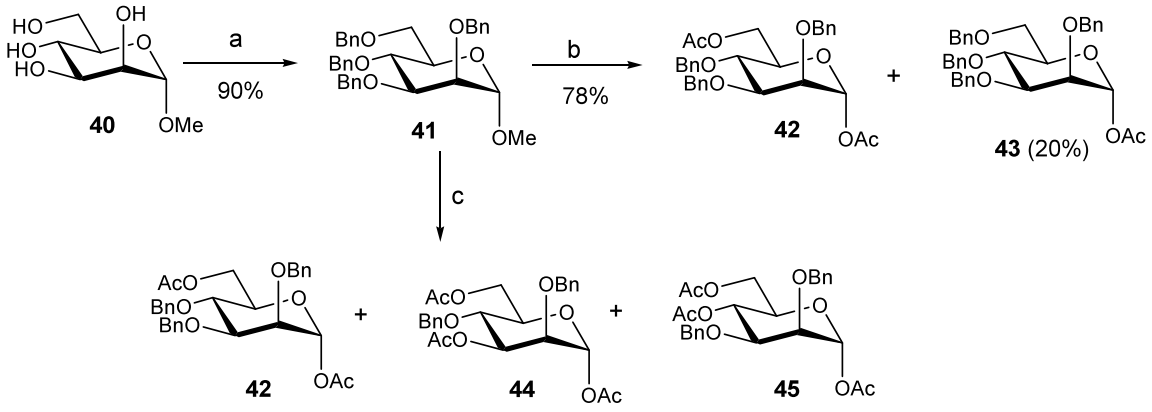


(a) $PhCH(OMe)_2$, $TsOH.H_2O$, DMF, 1 hr, 60 ^oC; (b) BnBr, NaH, TBAI, DMF; (c) Ac_2O, TEA, DMAP, CH_2Cl_2, 1 hr; (d) Bu_4NHSO_4, BnBr, NaOH, CH_2Cl_2, reflux; (e) BH_3·THF, $Cu(OTf)_2$, CH_2Cl_2, 2.5 hr; (f) BzCl, Et_3N, CH_2Cl_2, DMAP, 2.5 hr

Scheme 9: Synthesis of phenylthio-α-D-mannopyranose donors

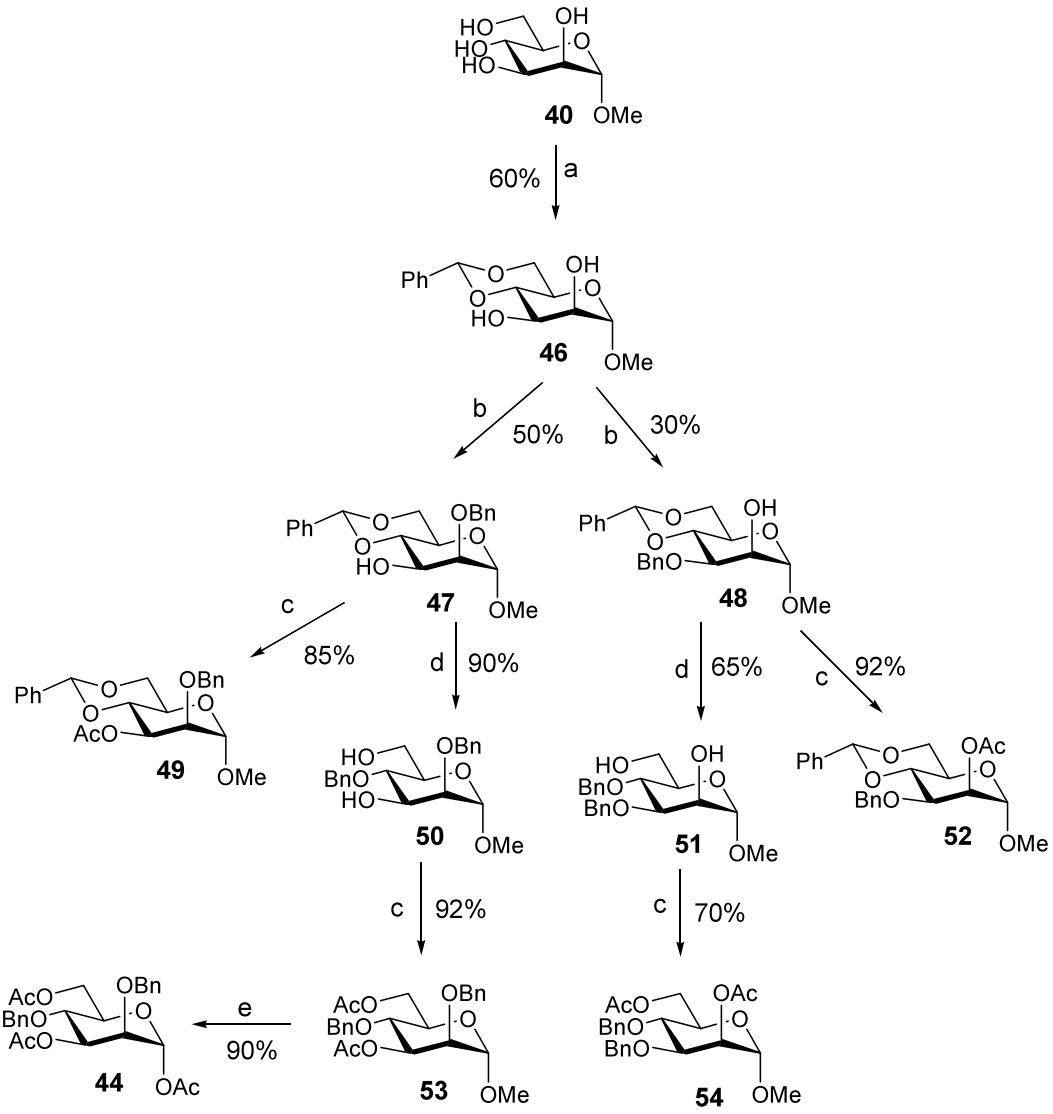
For the synthesis of acetyl-α-D-mannose donors (scheme 10), commercially available methyl α-D-mannopyranoside **40** was subjected to benzylation to give compound **41**. Selective acetylation of **41** using concentrated sulfuric acid as catalyst, gave **42**[107] and **43**. When a larger amount of acid was used in the same reaction, donors **42**, **44,** and **45,** respectively, were obtained.

As shown in scheme 11, the commercially available methyl α-D-mannopyannoside **40** was also used to generate many other compounds. The 4-,6-positions were protected as a benzylidene acetal to give **46** which was then selectively benzylated to give two distinct acceptors **47** and **48**. Acetylation of **47**[108] and **48** gave compounds **49** and **52,** respectively. Also, selective deprotection of the benzylidene group of **47** and **48** using borane-tetrahydrofuran complex gave **50** and **51,** respectively. Acetylation of **50** gave **53,** which was then converted to donor **44**. Also acetylation of **51** gave **54**.



(a) BnBr, NaH, TBAI, DMF; (b) Ac_2O, AcOH, H_2SO_4 (5 drops) , CH_2Cl_2, 0 ^oC, 5 hr
(c) Ac_2O, AcOH, H_2SO_4 (1.5 ml) , CH_2Cl_2, 0 ^oC, 5 hr

Scheme 10: Synthesis of acetyl-α-D-mannopyranose donors



(a) $PhCH(OMe)_2$, $TsOH.H_2O$, DMF, 1 hr, 60 °C; (b) Bu_4NHSO_4, BnBr, NaOH, CH_2Cl_2, reflux, 8 hr
(c) Ac_2O, TEA, DMAP, CH_2Cl_2, 1hr; (d) BH_3·THF, $Cu(OTf)_2$, CH_2Cl_2, 2.5 hr; (e) Ac_2O, AcOH, H_2SO_4, CH_2Cl_2, 0 °C, 3 hr

Scheme 11: Synthesis of methyl-α-D-mannopyranose derivatives

II.4 Solvent effect on the stereoselectivity

The primary goal was to determine the effect of solvents and protecting groups on the stereoselectivity of sonication assisted glycosylation. However, despite numerous attempts, the solvent effect on the stereochemistry is still unclear. Both 2-*O*-acyl and 2-*O*-alkyl groups favor the formation of α-glycosidic bond via neighboring group participation and anomeric effect, respectively.

Mannose is well known for its stereochemistry, which is predominantly the α-anomer. Extreme conditions have to be met in order to prepare the β-anomer. Crich proposed a general glycosylation mechanism using phenylthiomannosides as donors and 1-benzenesulfinyl piperidine (BSP) and triflic anhydride as the activating agents for the preparation of β-anomers.[109] In the proposed mechanism of this reaction, the α-mannosyl triflate intermediate is in equilibrium with a β-selective contact ion pair (CIP) and an α-selective solvent separated ion pair (SSIP) (figure 18). It is likely that sonication provides energy which facilitates an S_N2-like glycosylation through intermediate A or the contact ion pair (CIP) respectively, which will lead to the formation of β-mannosides.

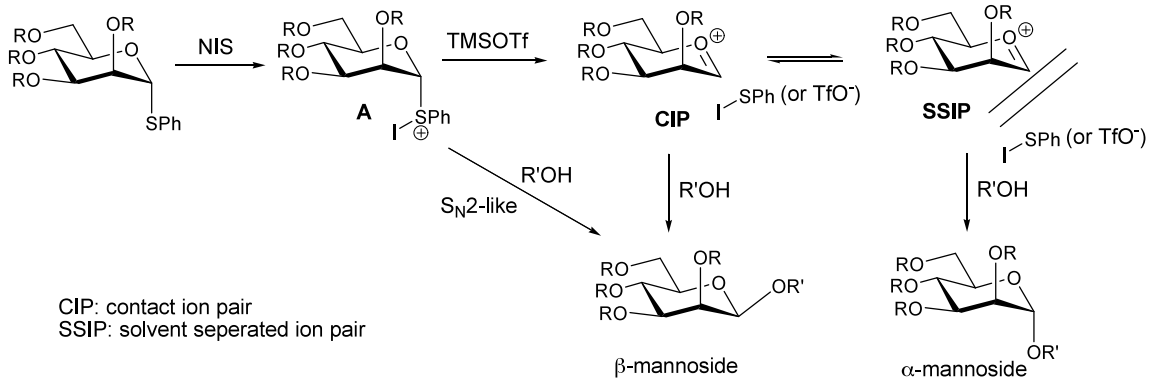
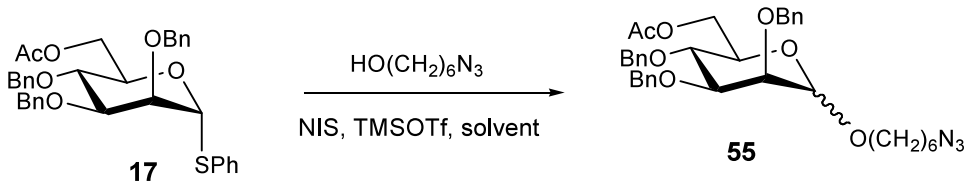


Figure 18: Proposed glycosylation mechanism

To carry out this study, compound **17** and 6-azidohexanol[78] were chosen as the donor and acceptor respectively (scheme 12). Compound **17** does not contain any participating groups on C-2 or C-3, which have been shown to always favor the α-anomer. 6-azidohexanol was chosen because after attachment of the sugar, the azide group will be reduced to an amine group. The amine group could then be used as an attachment point for a carrier protein to facilitate delivery into the body. Among the different solvents examined, there was no outstanding preference in the stereoselectivity under our sonication-assisted protocol.

Despite the difficulty in obtaining the β stereoisomer over α stereoisomer under sonication, it is evident that sonication can enhance the efficiency of glycosylation (entries 5 – 10, Table 1). The stereoselectivity of the products obtained was confirmed by $^{1}J_{CH}$ using HETCOR experiment. The most important carbon that was evaluated was the carbon at the anomeric center C-1. $^{1}J_{CH}$ values ranging from 158 – 165 are attributed to β stereoisomers while those that range from 168 – 180 are attributed to α stereoisomers.

As shown in Table 1, all the different solvents used gave both α- and β-anomers. However, traditional glycosylation (-78 ^{o}C to RT) which does occur in less polar solvents like toluene and ether, gave modest to excellent yields under sonication. A mixture of solvents (entry 9) was also used, but the result was the same, as both anomers were obtained. Though no selectivity was observed under sonication conditions, the formation of the β-anomer in the presence of a non-participating group on C-2 (such as benzyl group) was observed, leading us to believe that this reaction undergo a different type of mechanism under sonication.



Scheme 12: Coupling of **16** with 6-azidohexanol

Table 1: Effects of solvent on the stereoselectivity

Entry	Solvent	Condition	Yield (%)[a]	α/β ratio
1	Toluene	-78 °C – RT, 5 hr to overnight	No reaction	-
2	Et_2O[b]		No reaction	-
3	CH_2Cl_2		90%	1/1
4	CH_3CN		98%	3/2
5	Toluene	Sonication, rt 8 min	80%	2/1
6	Et_2O		40%	1/1
7	CH_2Cl_2		92%	3/2
8	CH_3CN		65%	3/2
9	Toluene/dioxane (1:1)		90%	1/1
10	CH_2Cl_2	NIS, BF_3-OEt_2 Sonication, 8 min	80%	3/1

[a]: isolated yield, [b] : no reaction even after heating (30 – 40 °C) for 5 hr

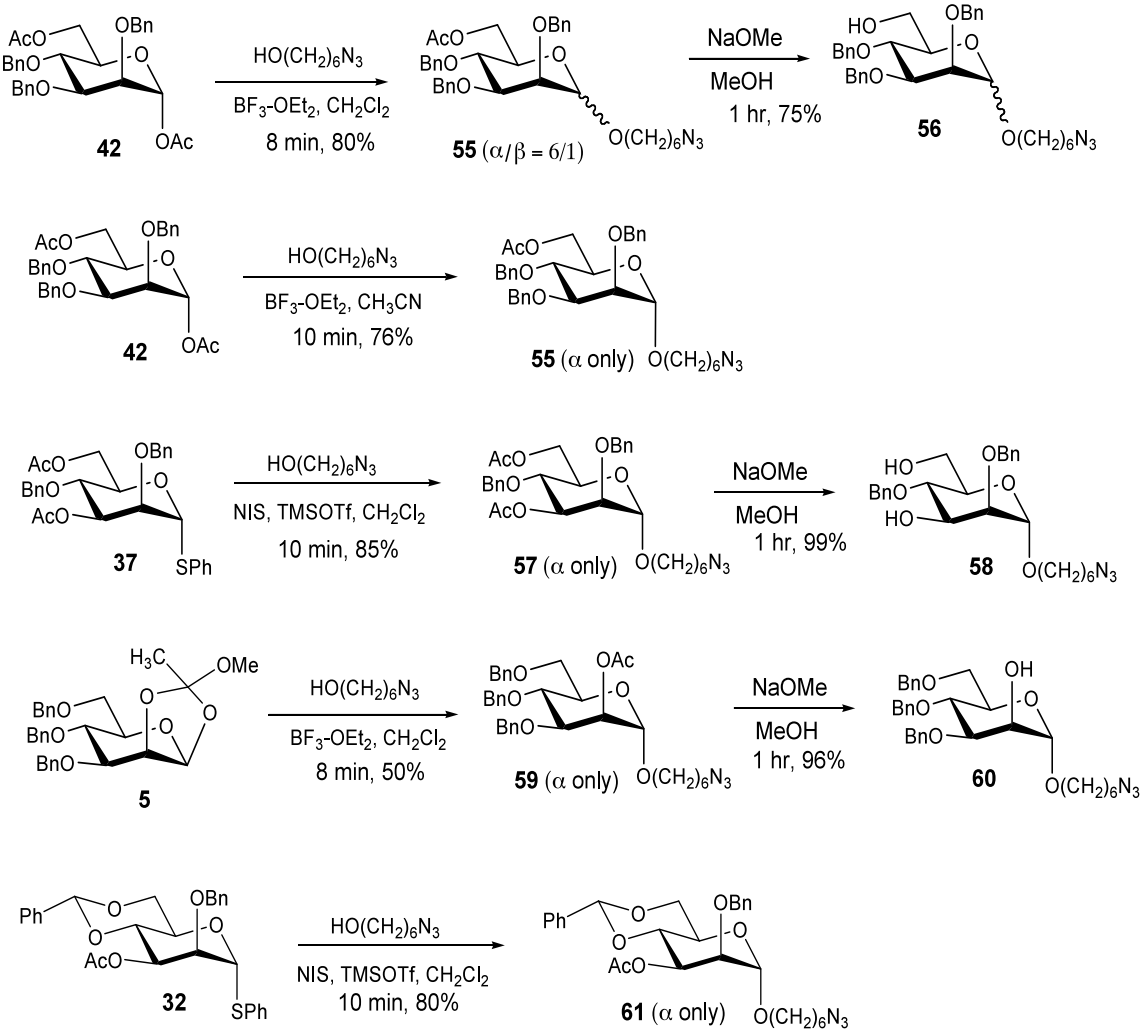
II.5 Synthesis of monosaccharides with 6-azidohexanol

Several mannose donors including glycosyl acetate, thiophenyl glycosyl and the orthoester donor, were examined under sonication. They are known to have low reactivity under traditional glycosylation conditions. All the monosaccharides were prepared using a single glycosyl acceptor which is the 6-azidohexanol and the time needed to complete these reactions was between eight to ten minutes (scheme 13).

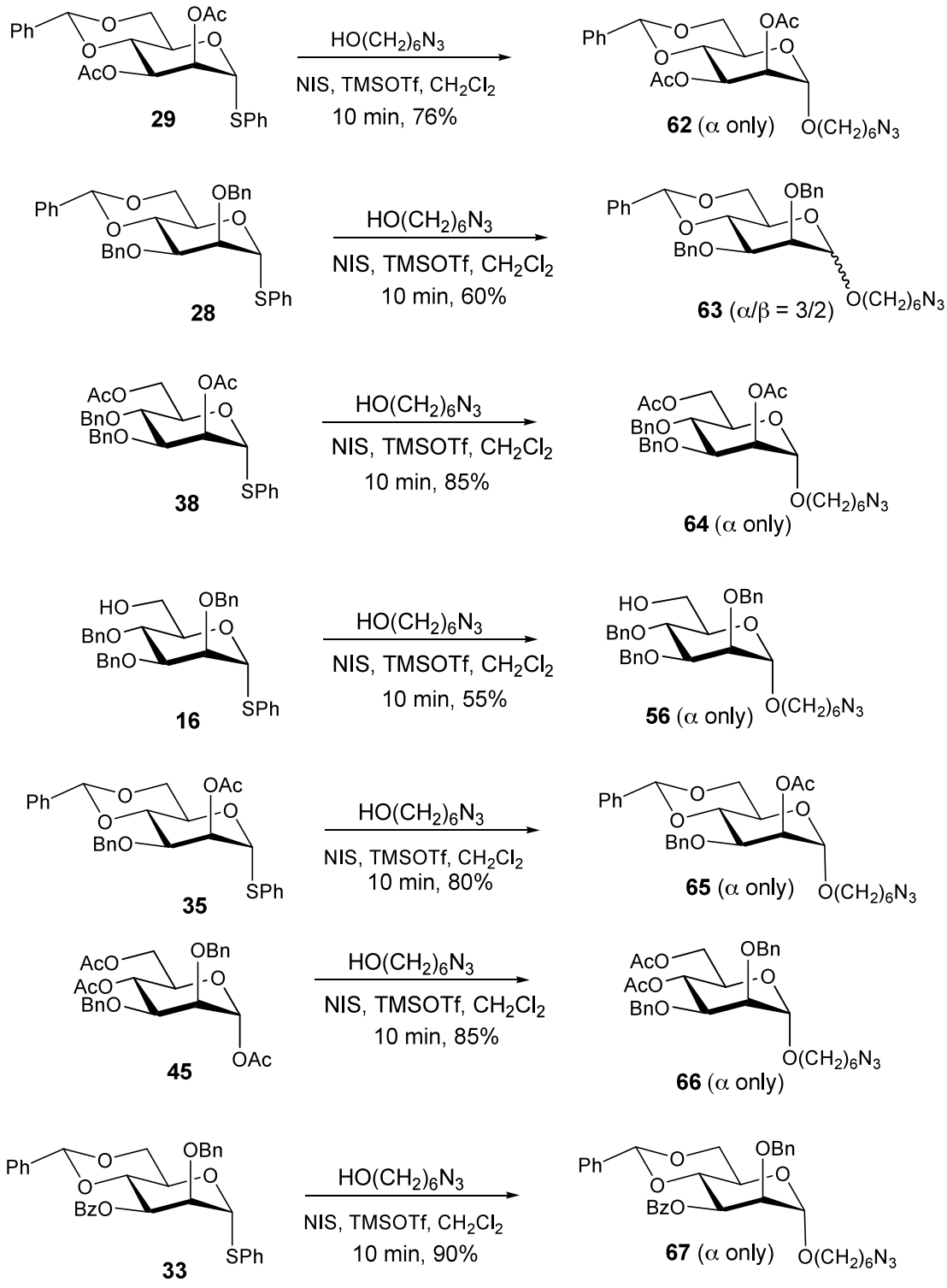
Acetate donor **42** was glycosylated in eight minutes to give **55** with α/β ratio of 6/1, when using CH_2Cl_2 as the solvent but when the solvent was changed to CH_3CN, only α-selectivity was observed. This could be due to the solvent used or simply the fact that the other isomer was not isolated during purification but no reasonable explanation can account for the observed selectivity at this point. There is a great difference nevertheless in the products obtained when using thiophenyl donors compare to acetate donors. Methanolysis of **55** gave **56**. Sonication using the thioglycosyl donor **37** gave **57** as a single α-anomer and treatment with NaOMe in MeOH gave **58**. As stated earlier, this shows that electron withdrawing groups at C-3 also have an effect on the stereochemistry of product. Glycosylation with orthoester donor **5** gave **59** which was further treated with NaOMe in MeOH to give **60**. The benzylidene protected donor **32** which usually gives the β-anomer under extreme traditional conditions, gave α-anomer **61**. While the benzylidene protected donor **29** also gave **62** with α-selectivity. **28** bearing no carboxylated group gave **63** as a mixture of α/β with the ratio 3/2. Thioglycosyl donor **38** also gave **64** as a single compound. Interestingly, glycosylation between two acceptors **16** and 6-azidohexanol gave a monosaccharide **56**. Formation of a disaccharide could be observed in this reaction. Treatment of donor thiophenyl **35** with 6-azidohexanol gave **65**.

Coupling of acetate donor **45** with the same alcohol gave **66** while thiophenyl donor **33** yielded **67** and all these reactions gave good yields under sonication.

As expected, glycosylation with *O*-2 acetyl participation gave only the α-anomer. Glycosylation with mannose bearing an acyl group at C-3 yielded predominantly α-mannosides. This selectivity has been explained by the neighboring group participation via a twist-boat conformation intermediate.[110]



Scheme 13: Investigation of sonication assisted glycosylation



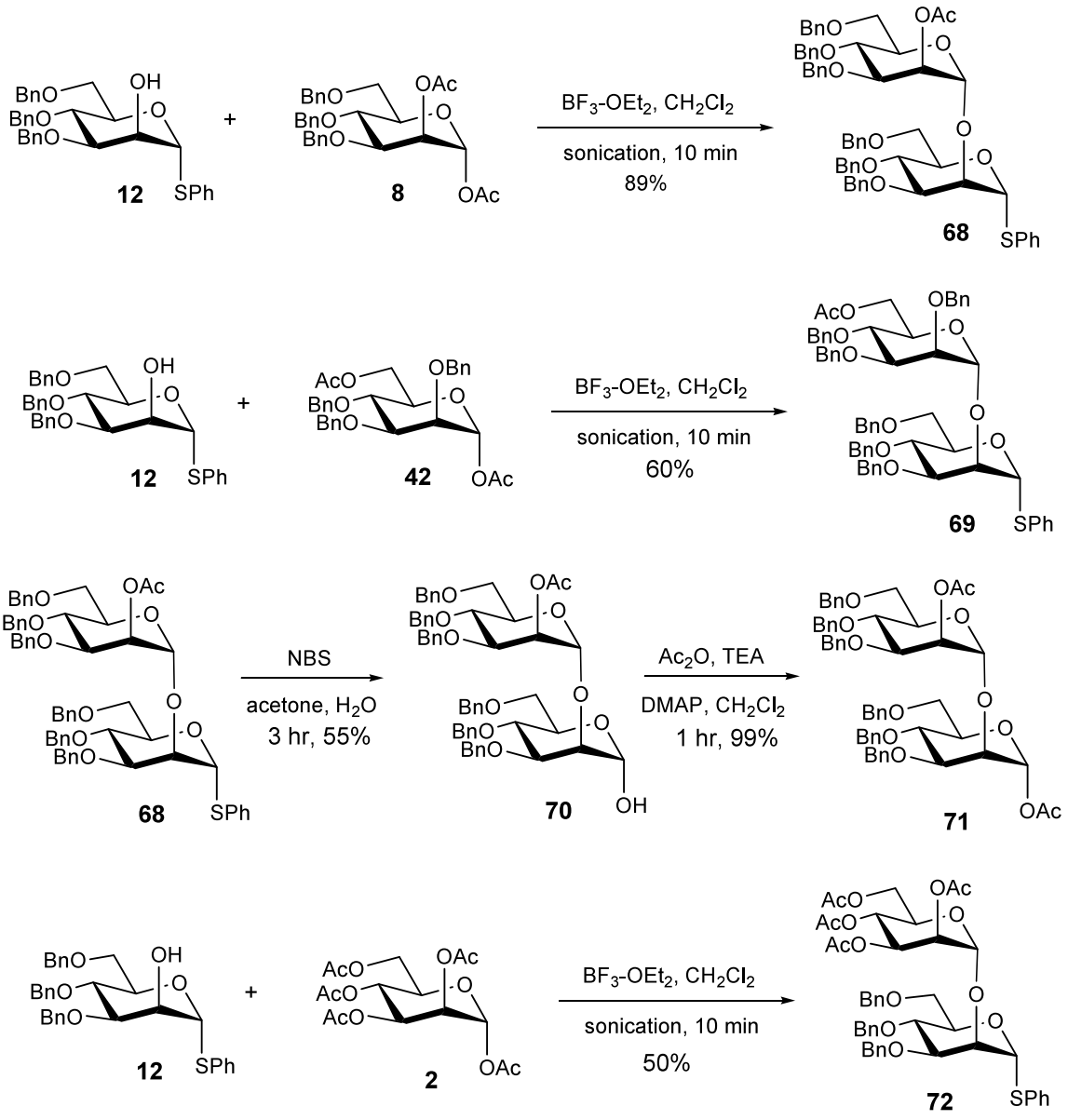
Scheme 13: Investigation of sonication assisted glycosylation (continued)

II.6 Synthesis of disaccharides

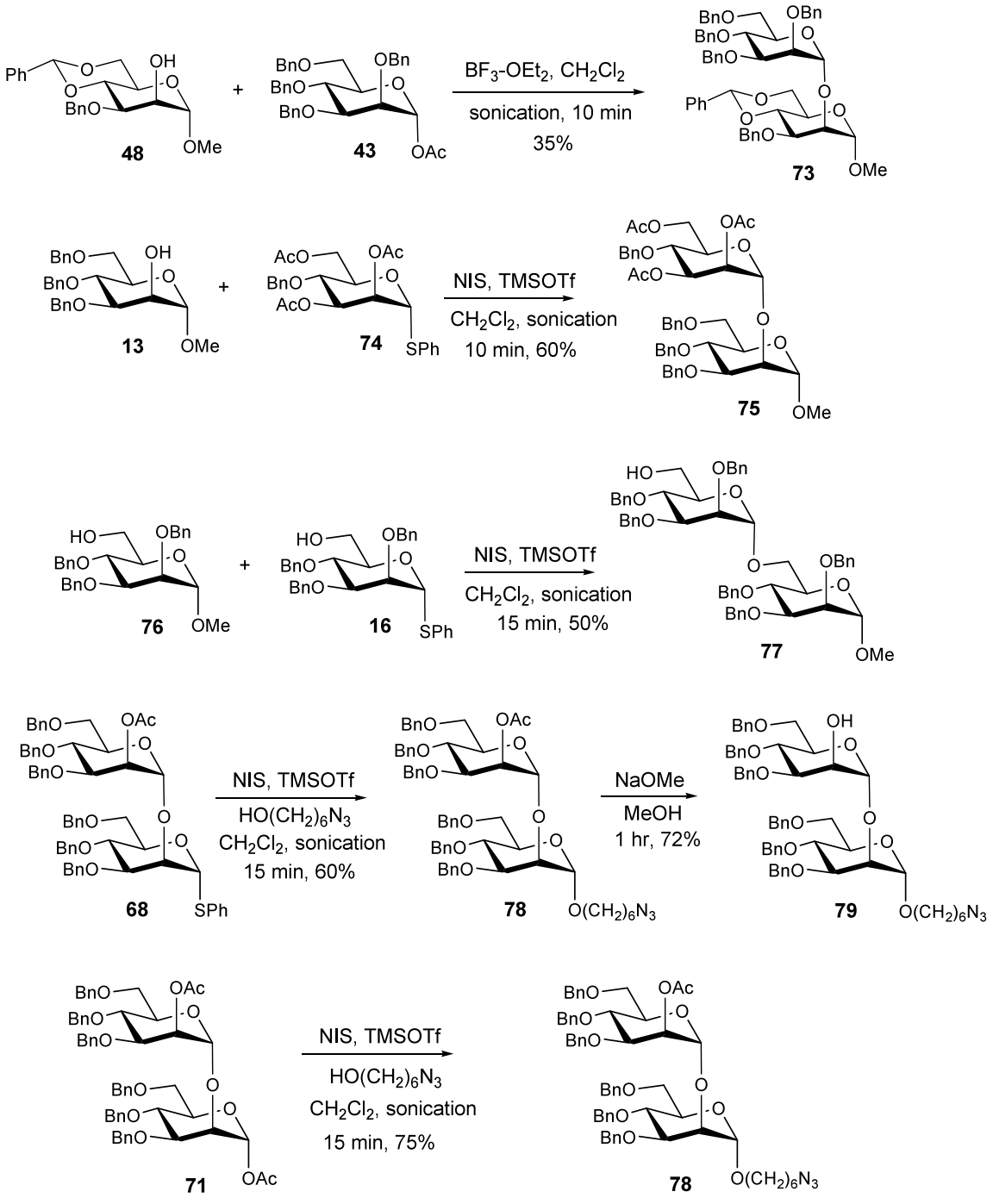
As well as synthesizing monosaccharide donors, it was envisioned envisioned that disaccharide donors (scheme 14) could be of great used in the synthesis of Man_9, one of our target molecules. Acceptor **12** was glycosylated with 1,2-diacetyl donor **8** to give thioglycosyl donor **68** with an acetyl group at the 2′ position. It was glycosylated with 1,6-diacetyl donor **42** as well to give donor **69** with an acetyl group at the 6′ position. Disaccharide donor **68** was also transformed to the corresponding acetyl donor, by treating with N-bromosuccinimide in acetone to give **70,** followed by acetylation to obtain the disaccharide acetyl donor **71**. Glycosylation of **12** with donor **2** gave donor **72.**

The synthesis of disaccharides gave solely α-anomers when the reactions were carried out with a secondary alcohol acceptor. No disaccharide β-anomer was isolated in these reactions as compared to reactions carried out with a primary alcohol acceptor.

The synthesis of some disaccharide compounds was also achieved with great success as can be seen in scheme 15. The coupling of **48** with **43** using a Lewis acid gave compound **73**. The coupling of **13** and thiophenyl donor **74** gave **75**. Glycosylation between two acceptors, **76**[111] and **16** gave the disaccharide **77**. Interestingly, sonication of the disaccharide donor **68** and **71** with 6-azidohexanol using the same conditions both gave the product **78**. Methanolysis of **78** gave **79**. Glycosylation using thiophenyl disaccharide donor under traditional conditions has rarely been successful when using NIS, TMSOTf. In order to activate this donor, several other reagents (AgOTf, PhSCl, AW 300, Et_2O/CH_2Cl_2) have to be combined together, but most often it is thiotoluene that has been used successfully with these reagents. But as shown in our protocol, this donor is very reactive and product is obtained in good yield.

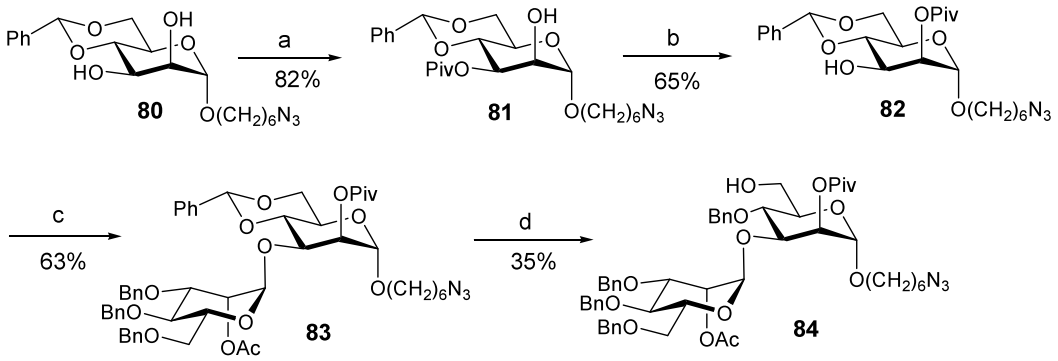


Scheme 14: Sonication assisted synthesis of disaccharides donors



Scheme 15: Sonication assisted synthesis of disaccharides compounds

As shown in scheme 16, the synthesis of **84** began from **80** with the selective protection of the secondary alcohol at C-3 over C-2 using pivaloyl chloride in basic medium to give **81**. Treatment of **81** with Bu_4NHSO_4 and benzyl bromide did not yield the desired product. Instead, migration of the pivaloyl group from C-3 to C-2 in **82** was observed. Coupling of **82** with donor **10** gave **83**. Unfortunately, treatment of **83** with copper triflate and borane-tetrahydrofuran complex to selectively open the benzylidene ring, gave **84** in low yield. This was a synthetic route aimed towards the synthesis of Man9, but was not pursued any further for this reason.



(a) PivCl, Py, 0 °C, 1 hr; (b) Bu_4NHSO_4, BnBr, NaOH, CH_2Cl_2, 5 hr; (c) **10**, NIS, TMSOTf, CH_2Cl_2, sonication, 15 min; (d) BH_3-THF, $Cu(OTf)_2CH_2Cl_2$, rt, 2.5 hr

Scheme 16: Synthesis of disaccharide compound **84**

II.7 Synthesis trimannosides

The synthesis of the trimannosides was designed and accomplished with the goal of doing some X-ray crystallography studies of the carbohydrate-protein interaction with a protein known as surfactant protein D (SP-D). Studies carried out on this protein with different sugars showed that SP-D binds strongest to D-mannose sugar and weakest to maltose and galactose under dynamic conditions.[112] This protein is a member of the collectin family of C-type lectins and binds carbohydrates in a calcium dependent manner. Several mannose binding protein (MBP)-carbohydrate complex structures, including complexes of MBP with several monosaccharides, have been determined by X-ray crystallography. It was found that SP-D recognizes carbohydrates by a mechanism similar to that of MBP.[113] Unfortunately for us, the results from the X-ray crystallography study were not completed in time for us to know how the interaction between the 1,6 and 1,2-linked trimannosides with SP-D occur.

II.7.1 Synthesis of 1,6-linked trimannoside

The synthesis of 1,6 linkages was accomplished with similar efficiency as with the synthesis for disaccharides using sonication (schemes 17 and 18). As stated earlier, $^{1}J_{CH}$ values obtained from HETCOR experiment were used to confirm the formation of the desired product. A mixture of both stereoisomer α and β was observed only when a glycosylation reaction was carried out between a primary alcohol and a donor. So the HETCOR experiment was very useful at this stage.

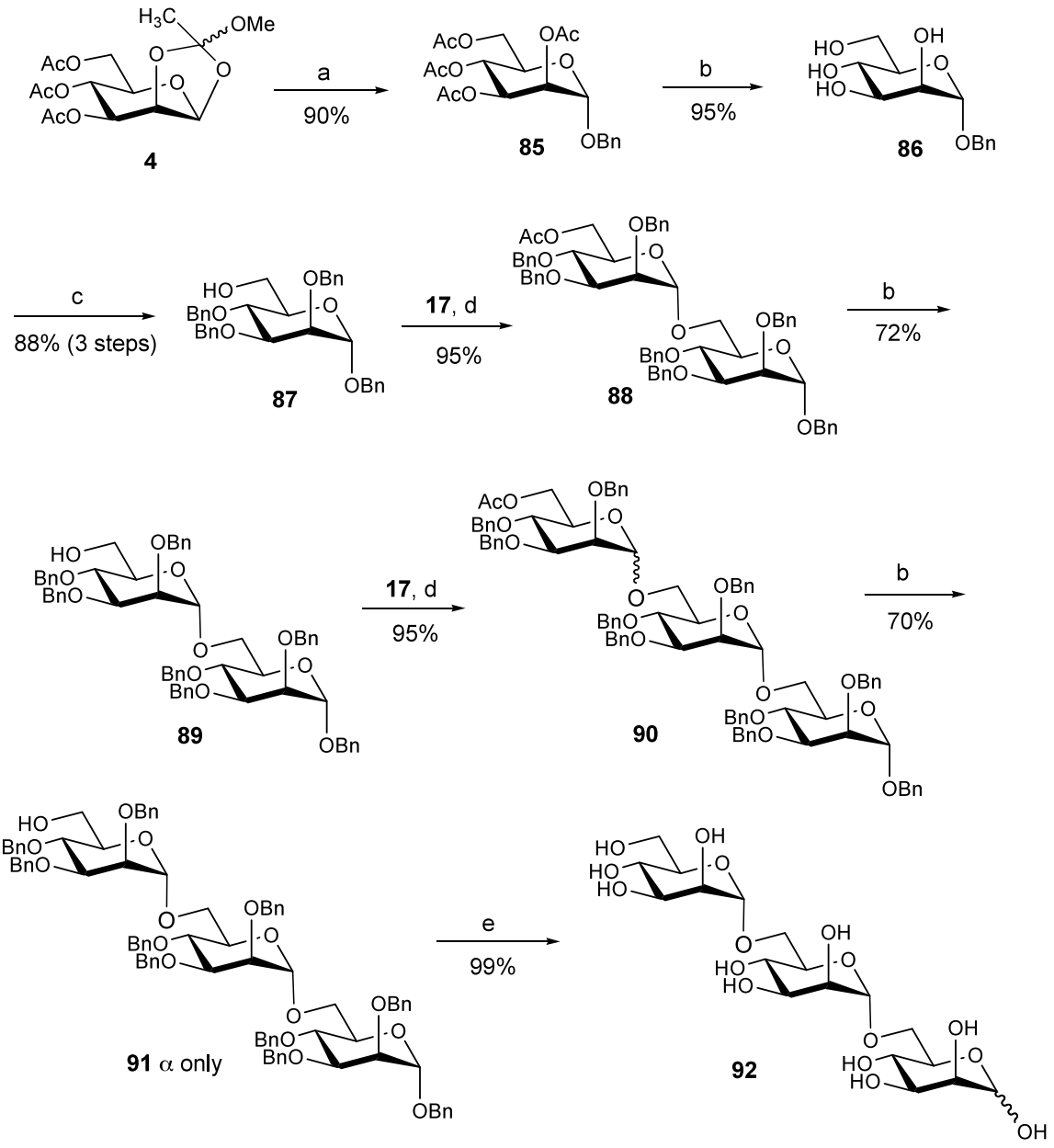
As shown in scheme 17, the orthoester **4**, was glycosylated with benzyl alcohol to give **85**. Methanolysis of **85** gave **86**. Selective protection of the primary alcohol at C-6 using trityl chloride, followed by benzylation and deprotection of the trityl group

afforded **87**[114] with a free hydroxyl group on C-6. Compound **87** was coupled with donor **17** to give **88**. Hydrolysis of **88** gave **89**, which was subjected to another glycosylation with **17** to give **90**. Methanolysis of **90** followed by global deprotection gave **92**. Glycosylation carried out on a primary alcohol with a donor having a nonparticipating group at 2 or 3-position, under sonication conditions gave a very small amount of the corresponding β-selectivity. Though difficult to separate after glycosylation with the protecting groups on, both anomers were easily separable after hydrolysis.

In scheme 18, α-methyl-D-mannoside **40** was treated with trityl chloride to selectively protect the primary alcohol at C-6, followed by benzylation and deprotection to give **76**. Acceptor **76** was glycosylated with donor **17** to give **93**. Treatment of **93** with NaOMe in MeOH gave **77** which was subjected to another glycosylation with donor **10** to give **94,** as a mixture of epimers. When **94** was subjected to methanolysis, the 2 epimers were separated to give **95** and *epi*-**95**. Global deprotection of **95** using deactivated palladium on carbon gave **96**.

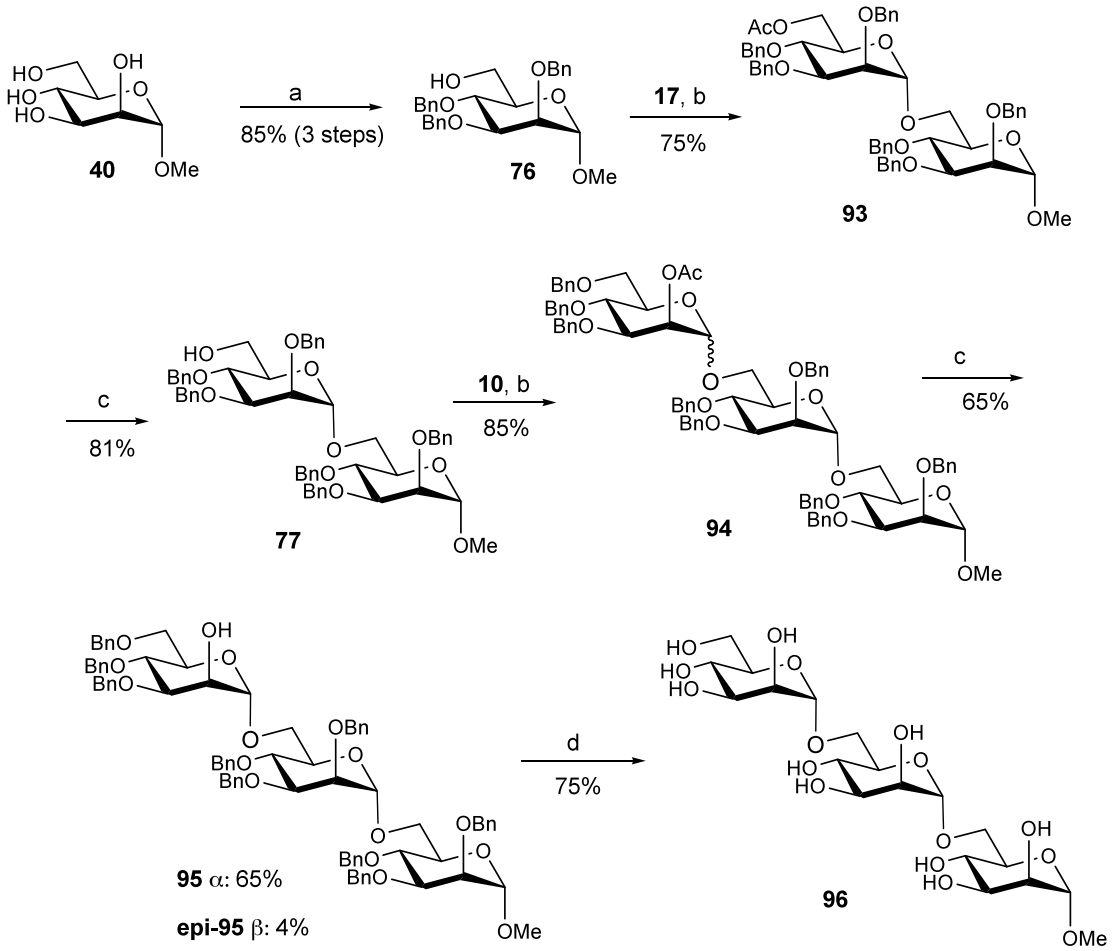
II.7.2 Synthesis of 1,2-linked trimannosides

The synthesis of **101** (scheme 19) began with glycosylation of acceptor **13** with donor **10** to give **97**. Methanolysis of **97** gave **98**, which was subjected to another glycosylation with **10** to give **99**. Another methanolysis of **99** followed by global deprotection gave **101**. The synthesis of another 1,2-trimannoside **108** (scheme 20) began with glycosylation of orthoester donor **5** with benzyl alcohol to give **102**.[115] Methanolysis of **102** followed by another glycosylation with donor **10** gave **104**. Methanolysis of **104** gave **105** which was subjected to another glycosylation with donor **17** to give **106**. General deprotection of **107** afforded **108**.



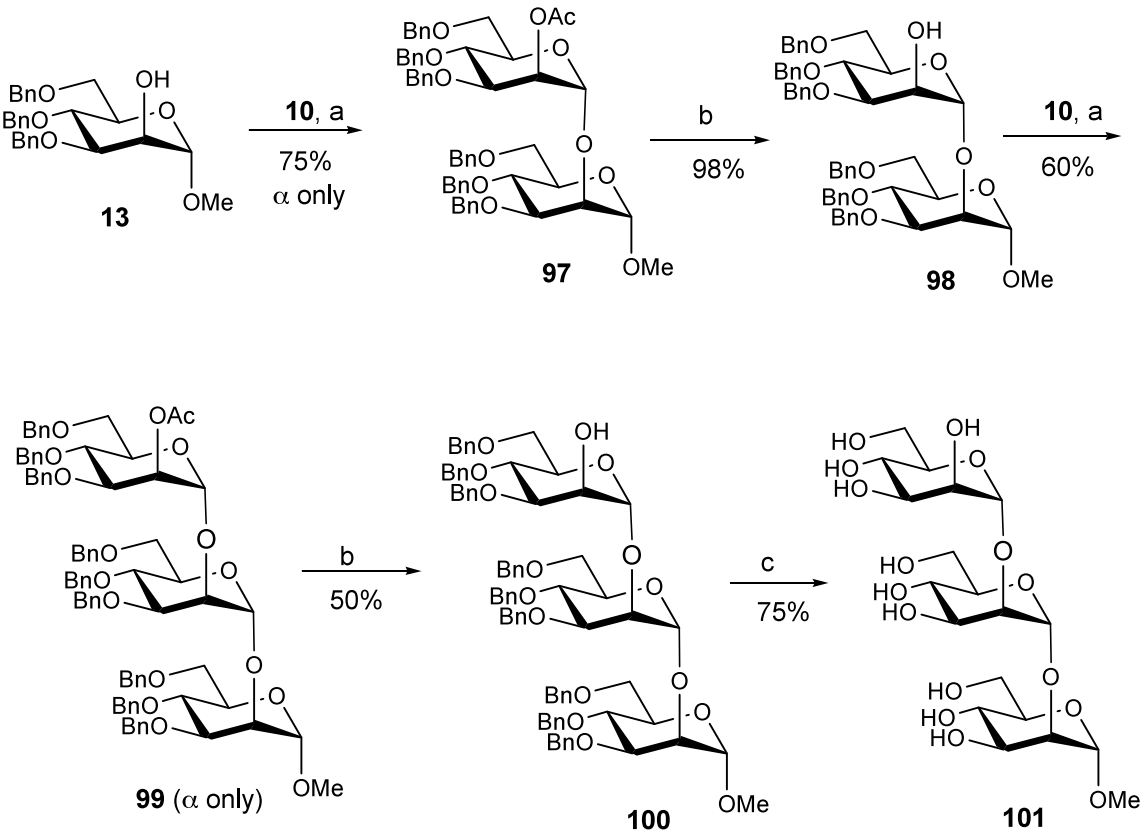
(a) BF_3-OEt_2, BnOH, CH_2Cl_2, sonication, 15 min; (b) NaOMe, MeOH; (c) i) TrCl, TEA, DMAP, CH_2Cl_2, ii) BnBr, NaH, DMF, TBAI, iii) $TsOH.H_2O$, CH_2Cl_2, MeOH; (d) NIS, TMSOTf, CH_2Cl_2, 10 min; (e) Pd(c), H_2, MeOH degased

Scheme 17: Synthesis of 1,6-linked trimannoside



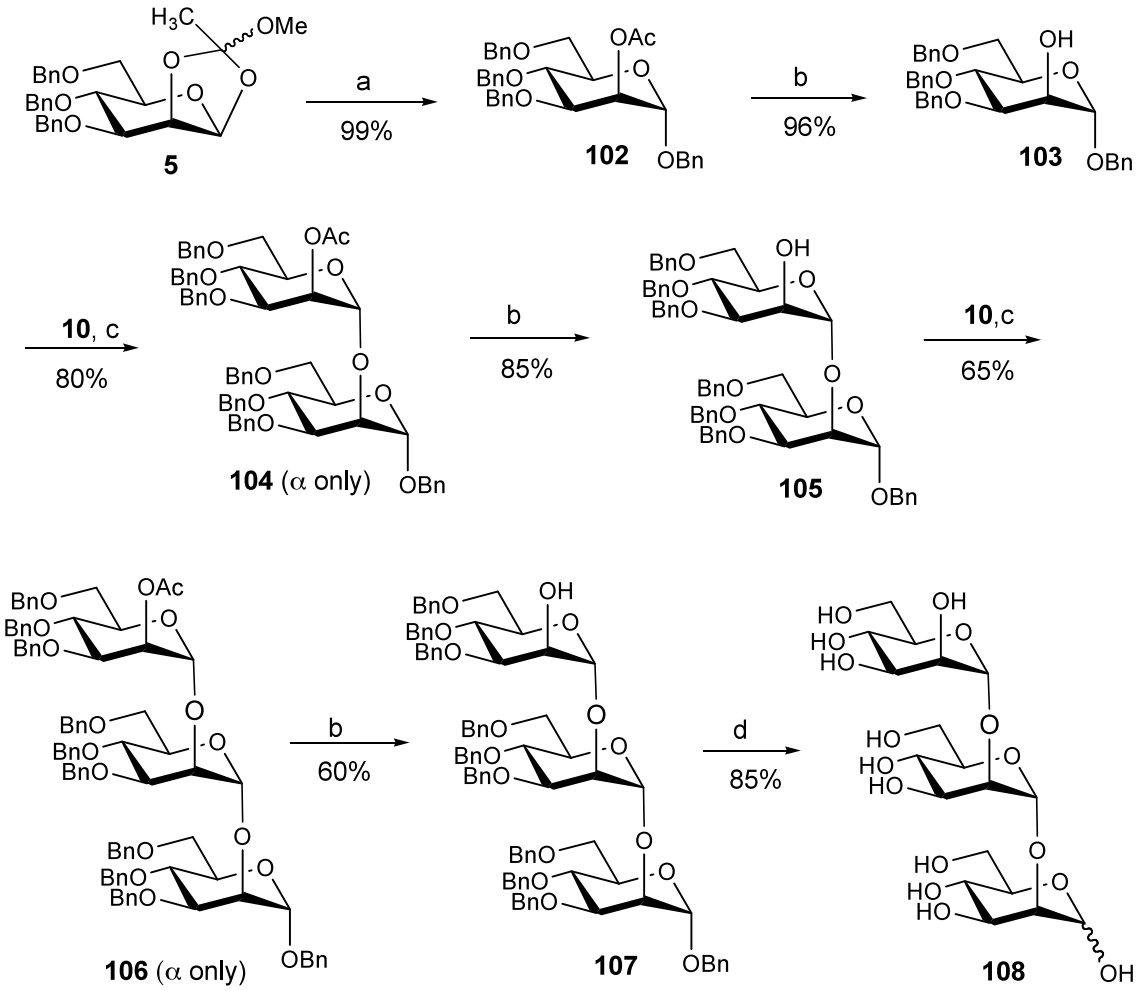
(a) i) TrCl, TEA, DMAP, CH_2Cl_2, ii) BnBr, NaH, DMF, TBAI, iii) $TsOH.H_2O$, CH_2Cl_2, MeOH;
(b) NIS, TMSOTf, CH_2Cl_2, 15 min; (c) NaOMe, MeOH; (d) Pd(C), H_2, MeOH degased

Scheme 18: Synthesis of methyl 1,6-linked trimannoside



(a) NIS, TMSOTf, CH_2Cl_2, 15 min; (b) NaOMe, MeOH; (c) Pd(C), H_2, MeOH degased

Scheme 19: Synthesis of methyl 1,2-linked trimannoside

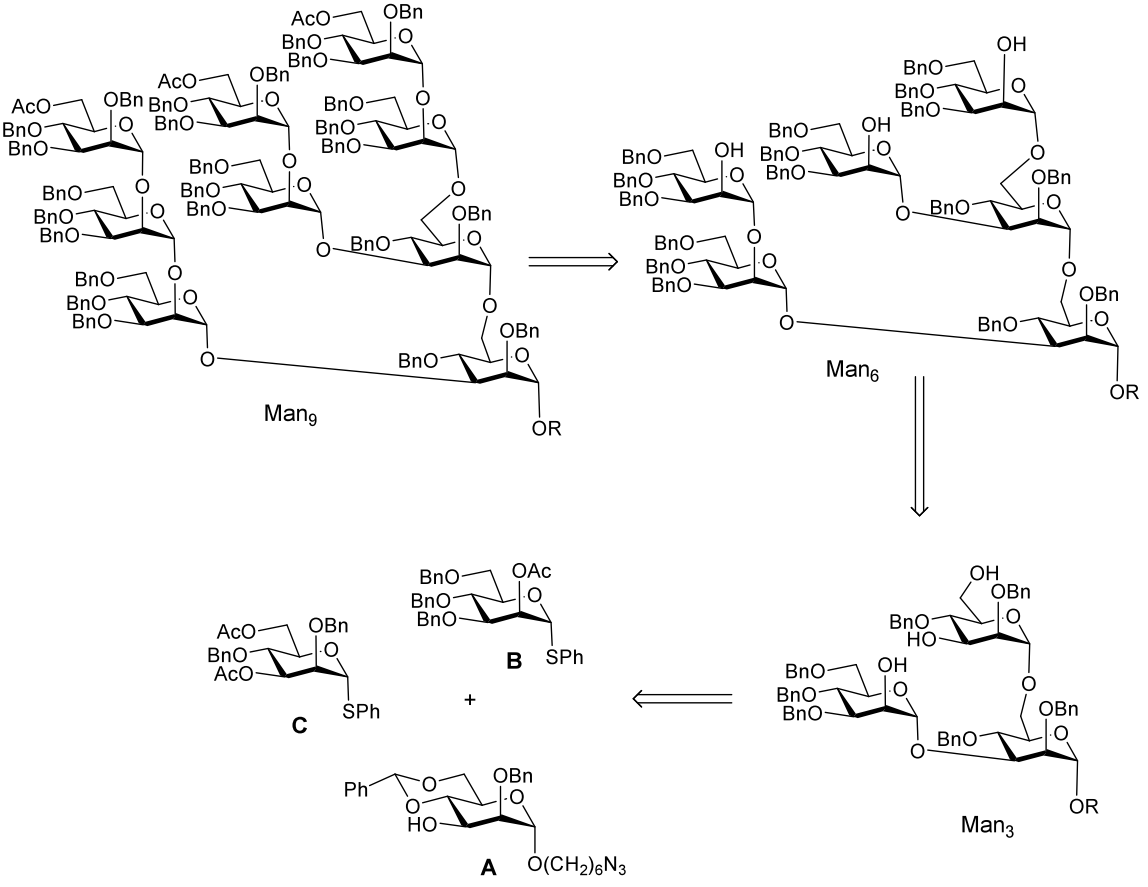


(a) BF_3-OEt_2, CH_2Cl_2, BnOH, 10 min; (b) NaOMe, MeOH; (c) NIS, TMSOTf, CH_2Cl_2, 15 min
(d) Pd(C), H_2, MeOH degased

Scheme 20: Synthesis of 1,2-linked trimannoside

II.8 Retrosynthetic analysis of complex oligomannoside

The synthesis of Man_9 was designed to follow the retrosynthetic scheme 21 below where Man_9 could be obtained from Man_6 which in turn could be obtained from Man_3. Man_3 will be obtained from glycosylation of fragment **A** with **B** followed by glycosylation with **C**.



Scheme 21: Retrosynthetic protocol of Man_9

II.9 Synthesis of Man_6

With success recorded in synthesizing di- and trimannosides, focus was then directed towards the synthesis of the more complex oligosaccharide, Man_6[116] considered as the prelude to the synthesis of Man_9, which has a potential of being used for HIV vaccine development. The synthesis of Man_6 (scheme 22) started with the coupling of acceptor **47** at C-3 with donor **10** to give disaccharide **109**. The 4,6-benzylidene protecting group in **109** was then selectively reduced to provide a primary alcohol in **110** using cupper triflate and boranetetrahydrofuran complex.[117] Disaccharide acceptor **110** was then coupled with donor **37** to give trisaccharide **111**. Hydrolysis of the acetyl groups in **111** gave acceptor **112** with three free hydroxyl groups. Trisaccharide **112** was again glycosylated with donor **10** to give hexammanoside **113**, followed by hydrolysis to obtain **114**. The synthesis of methyl-Man_6 using sonication conditions was very successful and the route was now applicable to a more complex oligomannoside Man_9, which is the oligosaccharide found on the surface of the gp120 glycoprotein of the HIV virus where it plays an important role.

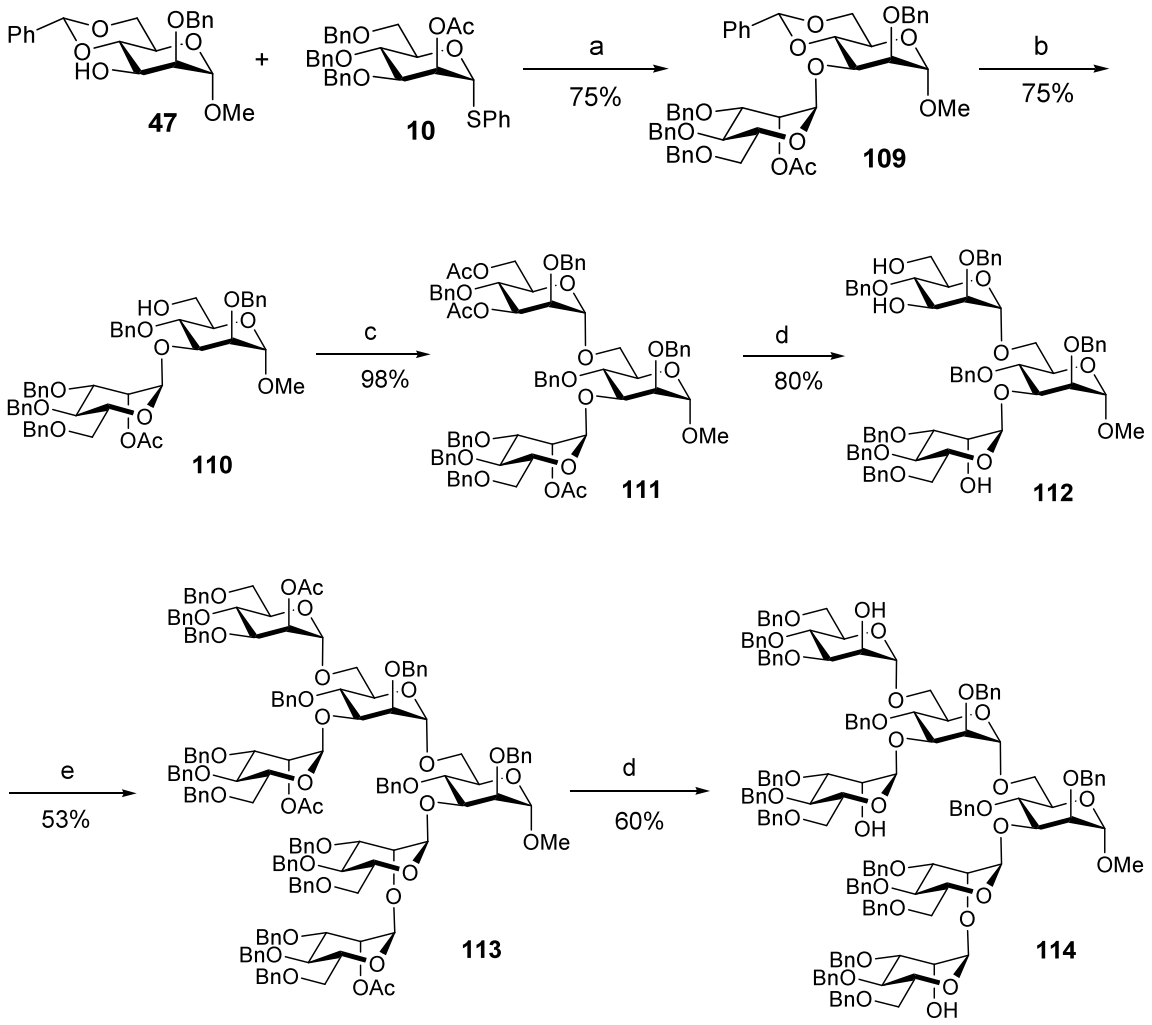
II.10 Synthesis of Man_9

The synthesis of Man_9 (scheme 23) began with glycosylation of pentacetylated mannose **2** with 6-azidohexanol to give **115**. Methanolysis of **115** using sodium methoxide in anhydrous methanol gave **116**. Selective protection of **116** using benzylidene acetal gave **80**. Selective benzylation of **80** using tetrabutylammonium hydrogen sulfate gave **117** (benzylated at C-2), and **118** (benzylated C-3). To differentiate between the two, both compounds **117** and **118** were acetylated to give 3-*O*-acetyl and 2-*O*-acetyl derivatives. Glycosyl acceptor **117** was then coupled with thioglycosyl donor **10**

to give disaccharide **119**. Selective deprotection of **119** afforded the primary alcohol **120,** and a diol **121**. The disaccharide **120** was then glycosylated with **34** to yield trisaccharide **122**. Methanolysis of **122** gave **123,** with three free hydroxyl groups. Trisaccharide acceptor **123** was then triglycosylated with **10** to afford hexamannoside **124,** which was treated with NaOMe in MeOH to yield **125**. This was again triglycosylated with **17** to afford **126,** which was subjected to hydrolysis, to give **127**. The conditions for the synthesis of Man_9 need to be optimized so that analogs could be synthesized. In order to let reactions go to completion under sonication conditions, excess donor needed to be used especially when dealing with large molecule with more than one hydroxyl group. Reactions carried out under these conditions were successful. The yields obtained were moderate to excellent, but some of the low yields were sometimes due to little material used. Sonication has proven to be reliable towards the synthesis of complex carbohydrates and more studies are needed to understand the stereoselectivity under this method.

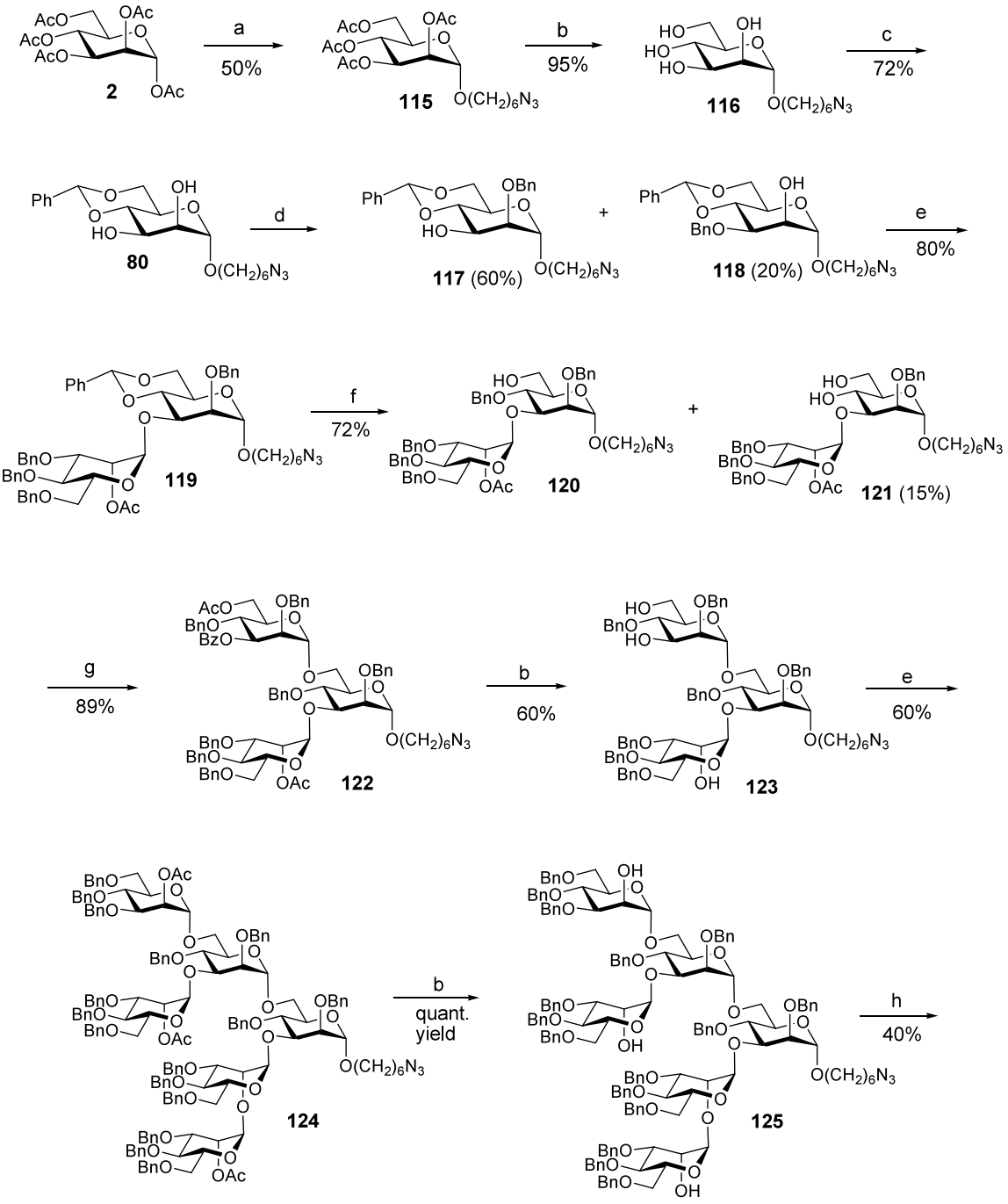
In summary, the synthesis of oligomannosides was achieved using sonication in a relatively short synthetic scheme with good yields. Glycosylation carried out using primary alcohol as acceptor, sometimes gave a mixture of α / β products. All glycosylation reactions carried out using secondary alcohols as the acceptor exclusively gave the α-anomer. Glycosylation reaction that were carried out with electron withdrawing groups at C-2 or C-3 gave only α-anomer which is consistent with the results obtained by other research group under traditional methods.[97] Glycosylation with acetyl donors preferentially gave the α-anomer whereas glycosylation with the acetyl

group would provide both anomers: α and β. Sonication has proven to be an efficient tool that improves the synthesis of oligosaccharides over traditional glycosylation methods.

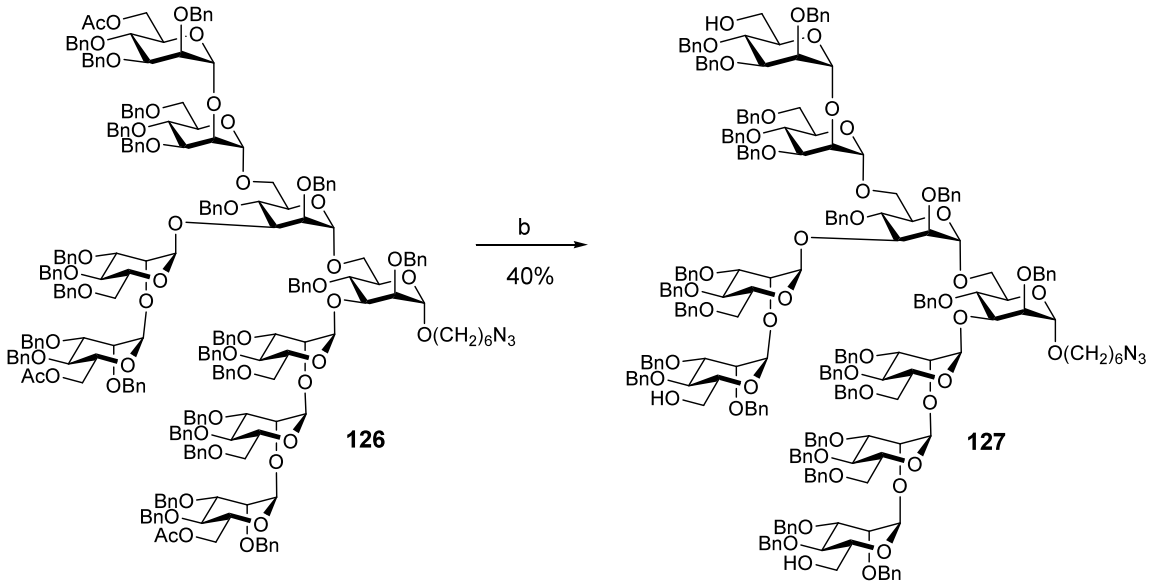


(a) NIS, TMSOTf, CH_2Cl_2, sonication, 10 min; (b) BH_3.THF, $Cu(OTf)_2$, CH_2Cl_2, 2 hr; (c) NIS, TMSOTf, **37**, CH_2Cl_2, sonication 15 min; (d) NaOMe, MeOH (e) NIS, TMSOTf, **10**, CH_2Cl_2, sonication, 15 min

Scheme 22: Synthesis of methyl- Man_6



Scheme 23: Synthesis of 6-azidohexyl- Man_9



(a) 6-azidohexanol, BF_3-OEt_2, CH_2Cl_2; (b) NaOMe, MeOH; (c) $PhCH(OMe)_2$, $TsOH.H_2O$, DMF, 60°C; (d) Bu_4NHSO_4, BnBr, NaOH, CH_2Cl_2; (e) NIS, TMSOTf, **10**, CH_2Cl_2, sonication, 10 min; (f) BH_3.THF, $Cu(OTf)_2$, CH_2Cl_2, 2 hr; (g) NIS, TMSOTf, **34**, CH_2Cl_2, sonication 15 min; (h) NIS, TMSOTf, **17**, CH_2Cl_2, sonication, 15 min

Scheme 23: Synthesis of 6′-azidohexyl-Man_9 (continued)

CHAPTER III

SOLID PHASE APPROACH SYNTHESIS

Over the past two decades, advances in technology have revolutionized the drug discovery process. The emergence of the high-throughput screening (HTS) techniques in pharmaceutical research has allowed biologists to design and set up assays (aimed toward the identification of active compound) that can rapidly test large numbers of compounds. This, therefore, requires high speed chemistry to provide these testing machines with compounds. If only traditional organic synthesis was to be used to provide biologist with these compounds, then chemists would have been faced with a huge challenge. Traditional methods are very time consuming and expensive, and thus incapable of feeding the fast paced biological testing procedures.

A new discipline called combinatorial chemistry, capable of significantly increasing the throughput of chemical synthesis in terms of diversity was developed to fulfill the HTS needs. Herein, very large numbers of compounds are synthesized by condensing small number of reagents together in all combinations defined by a given reaction sequence. Combinatorial chemistry can be used for either solution phase or solid phase techniques. Solid phase technique was introduced in the 1960s by Merrifield for the efficient synthesis of polypeptides[118] and has now become a standard technology for the preparation of oligopeptides and oligonucleotides, as well as small molecules to a lesser extent.

The most common solid support in solid phase synthesis is hydrophobic polystyrene (PS) resin beads. They are spherical microparticles and have different sizes

with reaction sites located both on the surface and within the beads. The bead diameter lies between 80 – 200 μm on average and the loading capacity which is the number of reaction sites is generally between 0.2 – 1.5 mmol/g.[119]

Solvation of the resins strongly influences the reactivity of the bead sites. The beads absorb solvents but remain insoluble and swell into gels in the course of a reaction. Swelling depends heavily of the solvent and on the percentage of cross-linking of the polystyrene support. Hydrophobic polystyrene resins swell properly in apolar solvent and their swelling is poor in polar protic solvents such as alcohols and water. Therefore, a good understanding of the swelling capacity of the resin in different organic solvents is the key to optimizing solution phase reactions for synthesis on the resin. For example, polystyrene swells to 8 ml/g resin in dichloromethane and hardly swells in methanol. Solvent and reagents move within the polymer matrix by diffusion. As most of the reaction sites on each resin bead are located inside the sphere, a good solvent for solid phase reaction will be one which can render the reaction sites accessible to reagents.

The use of a solid support to carry out organic chemistry has a profound influence on some of the reaction parameters;[120] above all there is a strong effect on the rate of the reaction. When a reaction takes place under traditional conditions, the reactants can freely interact and the reaction will depend on parameters such as temperature, concentration, etc. But when a resin-bound reagent is involved, the reaction will depend on the rate of diffusion of the reagent in solution into and out of the resin beads. Reaction rates are generally slower in solid phase chemistry than in solution phase. It is common to use excess reagents, in order to drive reactions to completion in solid phase synthesis compared to the solution phase synthesis.

Other than the reaction rate difference between solution phase synthesis and solid phase synthesis, another major difference is the work-up procedure for the reaction. During a solution phase synthesis, when the reaction is complete, it is quenched, then the workup to separate and purify the desired products from byproducts and other impurities. For a reaction carried out on solid phase, the reaction product remains attached to the resin while all the excess reagents and byproducts remain in solution. A typical workup will involve simple filtration of the resin followed by repeated washings with fresh solvents in which the resin swells well and the reagent and impurities are soluble.

Combinatorial organic synthesis, originally designed for peptide synthesis, has been favored by the availability of efficient and high-repetitive-yield synthetic protocols. Peptides are suitable for the construction of libraries due to the fact that a high degree of structural diversification can be easily achieved simply by varying the peptide sequence length or by introducing different amino acids other than the naturally occurring ones. Recent advances in this field have been extended to smaller organic molecules and reaction types.[121-124]

Several research groups have been involved in the solid phase synthesis of carbohydrates.[64,125] Major impediments to the growing field of molecular glycobiology is the lack of pure, structurally defined carbohydrates and glycoconjugates. These biomolecules are often found in low concentrations and in microheterogeneous forms in nature, greatly complicating their identification and isolation. The procurement of sufficient quantities of defined oligosaccharides required for detailed biophysical and biomedical studies therefore relies on efficient synthetic methods. Although much progress has been made in oligosaccharide synthesis,[126] the construction of complex

carbohydrates remains time consuming. The evolution of solid phase paradigm for the construction of oligosaccharide was initiated with Frechet's synthesis of di- and trisaccharides on polymer support in 1971.[127] Solid phase oligosaccharide synthesis has since seen many advancements. Although this has allowed for the construction of complex oligosaccharides, the manipulations remain tedious and time consuming. Also, the higher complexity of the sugar scaffold has prevented the development of a reliable solid phase procedure for the assembly of carbohydrate building blocks in a region- and stereospecific manner. In general, the multiple reactive sites and the stereochemical complexity have often hampered oligosaccharide synthesis and have prevented the growth of an automated technology for the solid phase synthesis of oligosaccharides.[128]

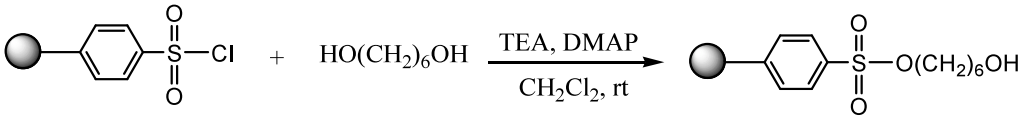
Following our success in the use of sonication in solution phase to synthesized oligosaccharides we extended the technique to solid phase synthesis as well. I chose polystyrene (PS) sulfonyl chloride resin for this project. They are also identified a catch and release resin. Another resin that could also be used will be the highly crossedlinked macroporous resin (MP). The PS resins require the use of solvents to swell the resin to permit reagents access to the functional groups while functional groups in the MP are already fully accessible. I decided to use the catch and release resins which are subset of the polymer reagents allowing the catching of a small molecule as an activated polymer intermediate, analogous to resin capture. The resin can be washed to remove soluble byproducts and then subjected to a second transformation to release the product. In this case, polystyrene toluene sulfonyl chloride (PS-TsCl), our resin of choice, is used to catch alcohols as polymer-bound tosylates. After workup involving resin washing, the

resin-bound tosylate is reacted with amines (in our case sodium azide) to release the amine products.

III.1 Solid phase synthesis of monosaccharides

The synthesis of monosaccharides was achieved using the less reactive acyl and thiophenyl glycosyl donors. It commenced with anchoring 1,6-hexanediol to the polystyrene sulfonyl chloride resin using TEA and DMAP in dichloromethane (scheme 24). This linker is stable to all the reaction conditions employed during the synthesis, prior to cleavage of the molecule from the resin, and can be selectively cleaved without compromising any part of the molecule. Once on the resin, the hexanediol with one hydroxyl group available is coupled to a donor, followed by cleavage from the resin with NaN_3 to give the product.

Several monosaccharides were synthesized using various sugars as donors and 6-azidohexanol as the acceptor (scheme 25), and both acetyl and thiophenyl donors were investigated. Interestingly all acetyl donors gave good results with yields ranging from 60 to 70%. The synthesis of fucose on the resin resulted in the α-anomer but when the reaction was carried out in solution, the β-anomer was obtained. This is quite a difference in the stereochemistry of this sugar. No mixture of both anomers was obtained.



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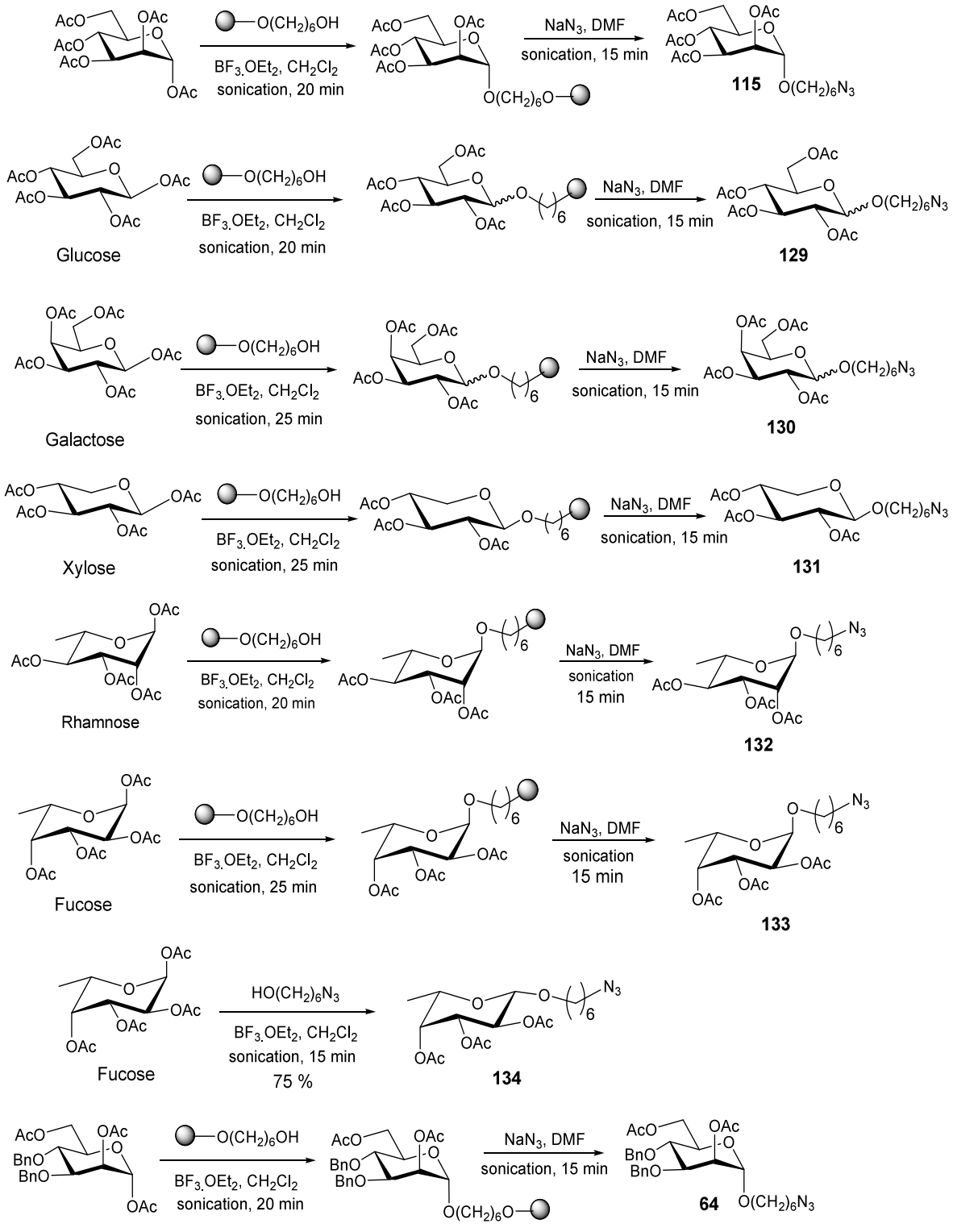
Scheme 24: Synthesis of resin acceptor



Scheme 25: Solid phase synthesis of monosaccharides

III.2 Solid phase synthesis of disaccharides

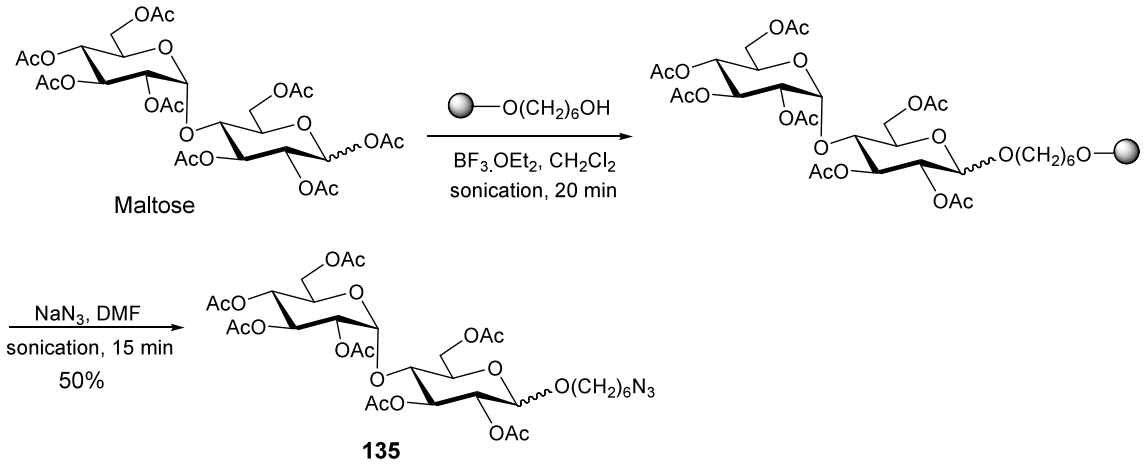
Preliminary test for disaccharide synthesis using both thiophenyl and acetyl donors revealed that moderate to good yields for the later and poor yields for the former. For this reason only reaction employing with acetyl donors were further pursued. Examples of these are presented in scheme 26 and 27.

Product analysis was carried out both on the resin (FT-IR on KBR disc) and in solution using NMR. Solution analysis required cleavage of the product from the resin after each step. This rendered the synthesis a little bit tedious as much resin was lost in the process. But this problem was alleviated by the use of FT-IR, which entailed using a few resin beads to prepare a KBr disc and recording the IR spectrum to estimate the degree of completion of reactions at the level of intermediates. This way, complete analysis (NMR) was employed only for the final products.

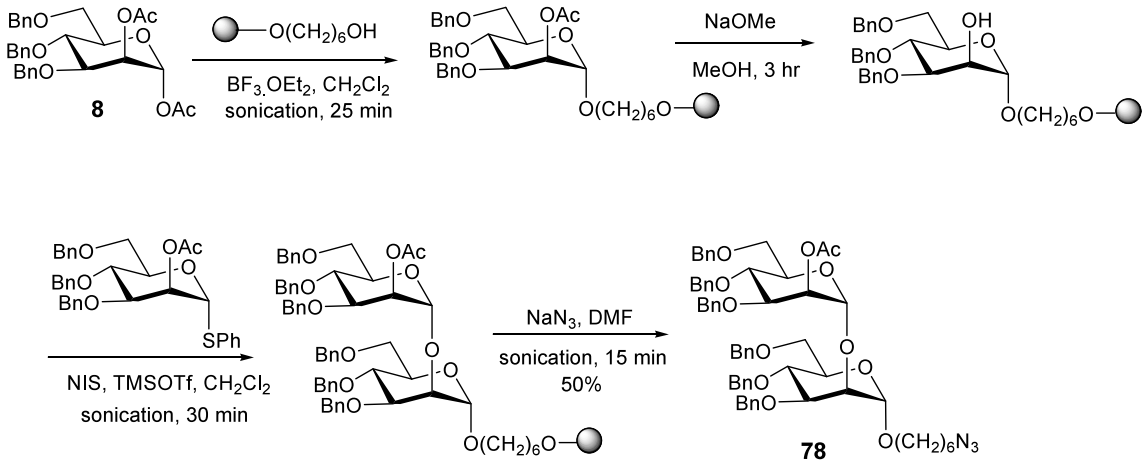
III.3 Solid phase synthesis of trisaccharide

Following the successful preparation of monosaccharides and disaccharidesusing a solid support, the study was extended to trisaccharides. To synthesize 1,2-linked trisaccharide (scheme 28), donor **8** glycosylated with 6-azidohexyl bound to the resin followed by methanolysis of the acetyl group. Disaccharide **69** was then coupled to the resin bound sugar to give **136**. Linear synthesis of this compound was not very good as the second sugar will always be cleaved off from the resin bound mannopyranoside.

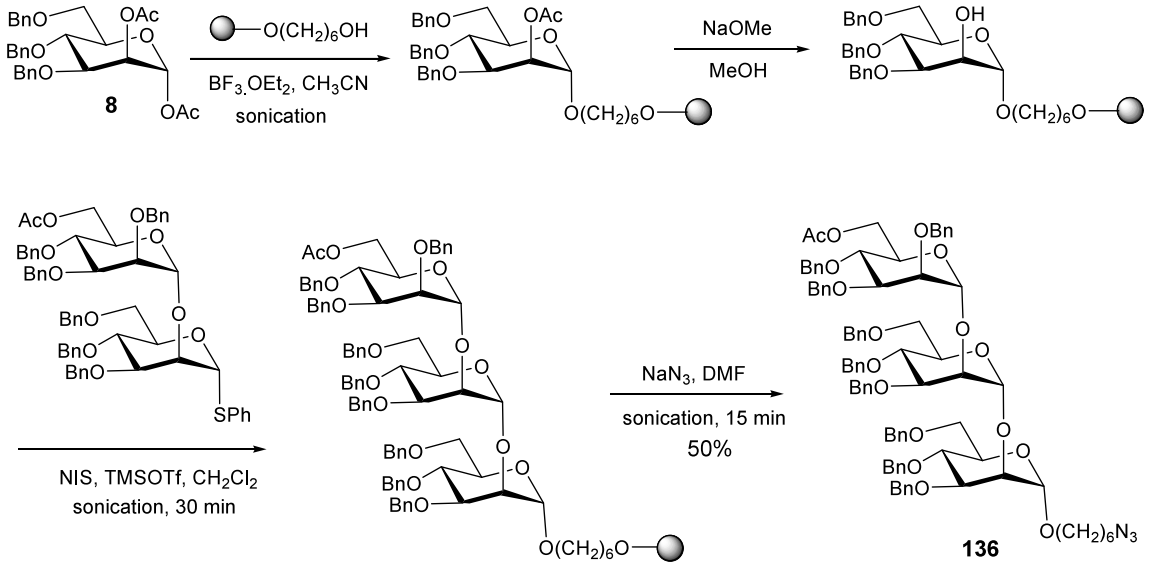
As shown in scheme 29, another trisaccharide was also synthesized by coupling compound **45** to the resin. After hydrolysis, the resulting compound was subjected to another glycosylation reaction, and when the resin was cleaved off, compound **137** was obtained.



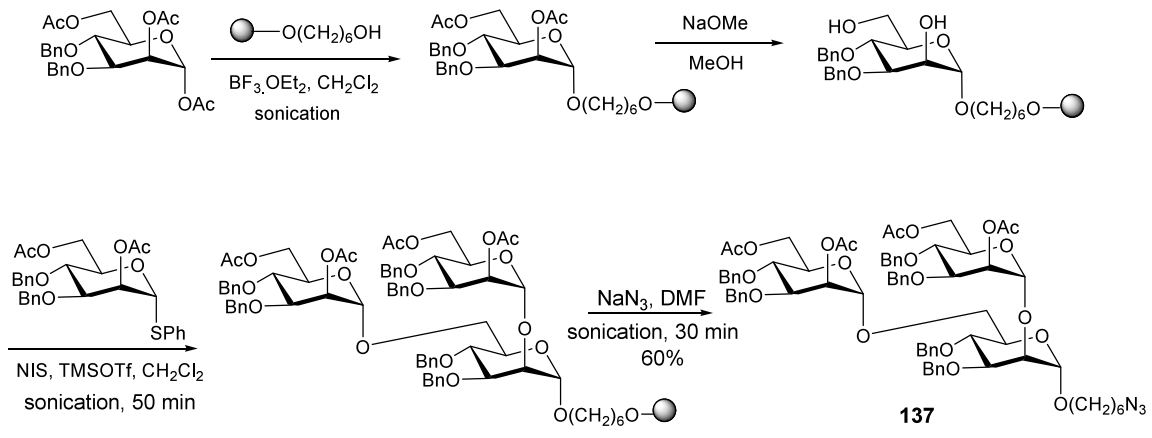
Scheme **26**: Solid phase synthesis of disaccharide **135**



Scheme 27: Solid phase synthesis of disaccharide **78**



Scheme 28: Solid phase synthesis of trisaccharide **136**



Scheme 29: Solid phase synthesis of trisaccharide **137**

III.4 Conclusions

The investigation of sonication as a new method for the synthesis of oligosaccharides has been achieved. The results obtained show that sonication can be used to synthesize carbohydrate compounds in good yields and much faster than the traditional methods. Solid phase approach under sonication has also proven to be quite successful even though more studies are needed to fully establish its usefulness.

We have been able to synthesize a variety compounds ranging from monosaccharides to oligosaccharides using sonication. Based on the desired stereoselectivity, donors with participating or non participating groups can be used to obtain target molecules in good yields and in record time.

CHAPTER IV

EXPERIMENTAL SECTION

Chemical reagents and chromatography solvents were reagent grade and used as purchased unless otherwise noted. Dichloromethane was freshly distilled from calcium hydride under nitrogen atmosphere. Pyridine and triethylamine were distilled and stored over 4Å molecular sieve. Column chromatographic purifications were carried out on silica gel 230x450 mesh, Sorbent Tech. Analytical TLC was performed on Sorbent Technologies silica gel glass TLC plates. Visualization was accomplished with UV light (254 nm) followed by staining with diluted sulfuric acid (5% in methanol) solution and heating.

Proton magnetic resonance spectra were recorded using JEOL 300, JEOL 270 or Bruker ARX 400 spectrometers. Chemical shifts were reported as parts per million (ppm) downfield from tetramethylsilane in δ unit and coupling constants were given in cycles per second (Hz). Signal multiplicities were indicated by s (singlet), d (doublet), t (triplet), and q (quartet). ^{13}C NMR spectra were obtained using JEOL 300 at 75 MHz, JEOL 270 at 68 MHz or Bruker 400 at 100 MHz. Sonication was conducted using Bransonic ultrasonic bath (model 5510) at 40 KHz with the power of 185 W.

General Procedure for glycosylation with thiophenyl donors

In a vial or flask, the acceptor (1 eq) and the donor (1.2 eq) were dissolved in CH_2Cl_2. NIS (1.2 eq) and TMSOTf (0.15 eq) were added respectively and the container was sealed with a septum and paraffin paper to prevent solvent from evaporating. The reaction mixture was then put into the sonicator at room temperature and time was

adjusted to 10 min. After 10 min, TLC was performed to check if the reaction was complete (if not then the reaction was sonicated again for 5 min). When complete, the reaction was poured into an Erlenmeyer flask containing $NaHCO_{3(S)}$ and $Na_2SO_{3(S)}$, and stirred for 30 min. When solution (dark red) turned yellow, it was filtered and washed with excess EtOAc, followed by removal of solvent and purification through a chromatography column. The product was obtained in a hexane/ethyl acetate gradient depending on the polarity. This includes compounds **55**, **56**, **57**, **61**, **62**, **63**, **64**, **65**, **67**, **77**, **78**, **83**, **88**, **90**, **93**, **94**, **97**, **99**, **104**, **106**, **109**, **111**, **113**, **119**, **123**, **125**.

General Procedure for glycosylation with acetyl donors

The acceptor (0.5g, 1 eq) is dissolved in 2 - 8 mL dichloromethane followed by addition of BF_3-OEt_2 (1 eq) and the mixture is closed with the septum plus paraffin and sonicated. Between 1 to 2 min while under sonication, the pressure in the vial is released by inserting a needle through the septum and then the acetyl donor (1.5 eq) already dissolved in dichloromethane is added slowly for about 1 min using a syringe. The reaction is then left to continue sonicating for the remainder of the time. When complete, the reaction is quenched with $NaHCO_{3(s)}$ and $MgSO_4.7H_2O$, after which the solids are filtered off, the filtrate is concentrated and purified through silica gel column. This includes compounds **55**, **68**, **69**, **73**, **78**, **115**.

General procedure for deprotection of acyl groups

The starting material is dissolved in anhydrous methanol and NaOMe (few drops) in anhydrous methanol is added and the mixture is stirred for 1 to 2 hours. When complete, the reaction is quenched by adding amberlite IR 120 H^+ resin to the mixture,

followed by filtration through celite, concentration of the filtrate and purification of the residue to afford the product. We have compounds **12**, **13**, **56**, **58**, **60**, **77**, **79**, **89**, **91**, **95**, ***epi*-95**, **98**, **100**, **103**, **105**, **107**, **112**, **114**, **124**, **126**.

General procedure for acetylation of compounds

The starting material is dissolved in dichloromethane followed by addition of acetic anhydride (2.5 eq), TEA (3.5 eq) and DMAP (cat amount). The mixture is stirred at room temperature for 1 hr after which the reaction is quenched by pouring into a flask containing saturated solution of sodium bicarbonate. The mixture is stirred until no bubbles are visible then it is diluted with ethyl acetate, washed with water, 1N HCl solution, $NaHCO_3$ and brine. The organic phase is dried over Na_2SO_4 followed by filtration, concentration and purification of the resulting residue through silica gel column. We have compounds **8**, **17**, **22**, **29**, **32**, **37**, **38**, **49**, **52**, **53**, **54**, **71**.

General procedure for selective deprotection of the benzylidene group

The starting material and copper triflate (0.15 eq) are dissolved in dichloromethane followed by slow addition of borane tetrahydrofuran complex (5 eq). The mixture is stirred for 2 hrs after which it is quenched with methanol. After stirring for some minutes, it is filtered through celite, concentrated and purified through a silica gel column. We have compounds **33**, **50**, **84**, **110**, **120**, **121**.

3,4,6-tri-*O*-acetyl-1,2-di-*O*-orthoester-β-D-mannopyranoside(4).[129] Compound **3** (2 g) was dissolved in toluene (10 mL) and anhydrous methanol (4 mL) was added and stirred under nitrogen. Silver oxide (1.5 g) was the added and the reaction mixture was stirred vigorously for 1 hr. Upon completion of the reaction by TLC analysis, the reaction

mixture was filtered through celite, concentrated. Purification by gradient column chromatography (hexane: EtOAc = 60:40 to 50:50) afforded the product as white crystals. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.50 (d, *J* = 2.6 Hz, 1H, H-1), 5.40 (t, *J* = 9.7 Hz, 1H, H-4′), 5.31 (t, *J* = 9.7 Hz, 1H, H-4), 5.27 (*J* = 2.3 Hz, 1H, H-1′), 5.20 (dd, *J* = 4.0, 9.8 Hz, 1H, H-3′), 5.15 (dd, *J* = 4.0, 9.8 Hz, 1H, H-3), 4.62 (dd, *J* = 6.6, 3.9 Hz, 1H, H-2), 4.39 (dd, *J* = 4.2, 2.4 Hz, 1H, H-2′), 4.25 (m, 2H, H-6, H-6′), 4.1 (m, 2H, H-6″, H-6‴), 3,70 (m, 2H, H-5, H-5′), 3.51 (s, 3H, OMe), 3.3 (s, 3H, OMe); 2.13 – 2.01 (m, 15H, 5 CH_3), 1.75 (s, 3H, CH_3), 1.55 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 170.7, 170.6, 170.5, 169.6, 169.5, 125.0, 124.7, 97.6, 95.0, 76.8, 75.7, 71.6, 71.4, 70.9, 70.8, 65.8, 65.6, 62.5, 62.1, 50.3, 50.1, 24.5, 24.2, 20.9, 20.9, 20.8, 20.7.

3,4,6-tri-*O*-benzyl-1,2-di-*O*-orthoester-β-D-mannopyranoside (5).[99] Compound **3** (4 g) was dissolved anhydrous MeOH (20 mL) and NaOMe/MeOH (0.5 mL) was added and the reaction mixture was stirred overnight. The next day when complete, the reaction mixture was concentrated and used directly. The resulting residue was dissolved in dimethylformamide (DMF) and cooled to 0 ^{o}C. NaH (3.5 g) was added and the mixture wascool to 0 ^{o}C and stirred under nitrogen for 10 min after which BnBr (6 mL) was slowly added followed by catalytic amount of TBAI and the reaction mixture was stirred over night. When the reaction was complete by TLC analysis, it was slowly quenched with methanol and stirred for another 1 hr. The residue was diluted with EtOAc, washed with water (x3), followed by 1N solution of HCl, $NaHCO_3$, water and brine then it was dried over Na_2SO_4. Removal of the solvent followed by purification through a silica gel column chromatography (hexane:EtOAc = 100 to 70:30) afforded compound **5** as 2

enantiomers **5a** and **5b** which were separable after column and which crystallized when dried over vacuum and compound **6** as oil with a gradient (hexane:EtOAc = 100 to 65: 35). **5a:** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.5 (m, 15H), 5.13 (d, *J* = 2.4 Hz, 1H, H-1), 4.96 (d, *J* = 10.6 Hz, 1H), 4.85 (d, *J* = 12.4 Hz, 1H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.68 (d, *J* = 10.6 Hz, 1H), 4.57 (s, 2H), 4.14 (dd, *J* = 1.7, 4.1 Hz, 1H, H-2), 4.07 (t, *J* = 9.3 Hz, 1H, H-4), 3.8 (m, 3H), 3.49 (s, 3H, OMe), 1.55 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.4 (2 carbons), 138.1, 128.65 (2 carbons) 128.60 (2 carbons), 128.4 (3 carbons), 128.2 (3 carbons), 128.17 (3 carbons), 127.9, 127.6, 127.5 (2 carbons), 124.3, 95.0, 79.4, 76.2, 76.1, 75.4, 75.0, 74.3, 74.1, 74.0, 73.6, 73.4, 72.5, 68.9, 50.3, 24.2;

5b: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 15H), 5.35 (d, *J* = 2.7 Hz, 1H, H-2), 4.90 (d, *J* = 10.6 Hz, 1H), 4.81 (d, *J* = 13.1 Hz, 1H), 4.77 (d, *J* = 13.1 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.61 (d, *J* = 10.4 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.40 (dd, *J* = 2.4, 3.8 Hz, 1H, H-2), 3.94 (t, *J* = 9.3 Hz, 1H, H-4), 3.7 (m, 3H), 3.4 (m, 1H, H-5), 3.29 (s, 3H, OMe), 1.75 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.3, (2 carbons), 137.9, 128.6 (2 carbons), 128.5 (2 carbons), 128.4 (2 carbons), 128.2 (4 carbons), 127.9, 127.6 (3 carbons), 124.1, 97.6, 79.1, 77.3, 75.4, 74.3, 74.2, 73.5, 72.5, 49.9, 24.6.

2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (6).[130] Please refer to the synthesis of compound **5**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.3 (m, 15H), 7.17 (m, 2H), 5.38 (dd, *J* = 1.9, 3.3 Hz, 2H), 5.22 (dd, *J* = 1.7, 3.8 Hz, 2H,) 4.88 (d, *J* = 10.9 Hz, 1H), 4.72 (d, *J* = 11.2 Hz, 1H), 4.62 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 11.2 Hz, 2H) 4.53 (d, *J* = 12.1 Hz, 1H), 4.48 (d, *J* = 10.9 Hz, 1H), 4.1 (m, 1H), 4.0 (m, 1H), 3.8 - 3.6 (m,

4H), 2.17 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 138.5, 138.1, 138.0, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 127.9, 127.8, 92.6, 77.9, 75.3, 74.8, 73.6, 71.9, 71.3, 69.5, 69.3, 21.4.

Acetyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (7). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.2 (m, 13H), 7.2 – 7.1 (m, 2H), 5.68 (d, *J* = 0.8 Hz, 1H, H-1), 4.87 (d, *J* = 10.8 Hz, 1H), 4.75 (d, *J* =11.6 Hz, 1H), 4.70 (d, *J* = 11.6 Hz, 1H), 4.66 (d, *J* = 12.2 Hz, 1H), 4.55 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 12.2 Hz, 1H), 4.16 (d, *J* = 2.5 Hz, 1H), 3.97 (t, *J* = 9.3 Hz, 1H, H-4), 3.2 (m, 2H), 3.68 (dd, *J* = 3.1, 9.1 Hz, 1H, H-3), 3.6 (m, 1H, H-5), 2.58 (s, 1H, OH), 2.18 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.2, 138.2, 138.1, 137.6, 128.7, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 92.6, 81.5, 76.0, 75.3, 73.6, 71.9, 68.6, 67.6, 21.1; ESI/APCI Calcd for $C_{29}H_{32}O_7Na$ ($[M+Na]^+$) m/z 515.2046; measured m/z 515.204.

Acetyl 2-*O*-acetyl-3,4,6-tri-benzyl-α-D-mannopyranoside (8).[100] ^1H NMR ($CDCl_3$, 400 MHz) δ 7.3 - 7.1 (m, 15 H), 6.16 (d, *J* = 2.0 Hz, 1H, H-1), 5.38 (dd, *J* = 4.72, 2.38 Hz, 1H, H-2), 4.84 (d, *J* = 10.6 Hz, 1H), 4,76 (d, *J* = 11.2 Hz, 1H), 4.72 (d, *J* = 12.2 Hz, 1H), 4.56 (d, *J* = 11.2 Hz, 1H), 4.52 (d, *J* = 10.6 Hz, 1H), 4.50 (d, *J* = 12.2 Hz, 1H), 3.8 (m, 2H), 3.8 (m, 2H), 3.65 (dd, *J* = 10.8, 1.6 Hz, 1H, H-6'), 2.18 (s, 3H), 2.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 168.5 138.4, 137.9, 128.6 (3 carbons), 128.6 (3 carbons), 128.5 (3 carbons), 128.15 (2 carbons), 128.08 (2 carbons), 128.06, 128.00 (2 carbons) 127.9, 127.8, 91.5, 77.9, 75.6, 74.1, 73.9, 73.8, 72.2, 68.8, 67.8, 21.2, 21.1.

Methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (11).[101] ^1H NMR ($CDCl_3$, 400 MHz) δ 7.2 – 7.4 (m, 15 H), 5.39 (dd, *J* = 3.1, 1.9 Hz, 1H, H-2), 4.84 (d, *J* =

10.8 Hz, 1H), 4.78 (d, *J* = 1.6 Hz, 1H, H-1), 4,72 (dd, *J* = 12.1, 4.4 Hz, 1H, H-3), 4.55 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 10.8 Hz, 1H), 3.98 (dd, *J* = 9.2, 3.4 Hz, 1H, H-6), 3.90 (t, *J* = 9.4 Hz, 1H, H-4), 3.82 (m, 1H, H-5), 3.78 (m, 1H, H-6'), 3.38 (s, 3H, OMe), 2.18 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 138.7, 138.5, 138.2, 128.6, 128.5, 128.3, 128.0, 127.9, 127.9, 127.8, 99.0, 78.4, 75.3, 74.6, 73.7, 71.9, 71.5, 69.2, 68.9, 55.1, 21.3.

Phenyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (12).[102] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48 (m, 2H), 7.2 – 7.4 (m, 18H), 5.63 (s, 1H, H-1), 4.86 (d, *J* = 10.8 Hz, 1H), 4.73 (s, 2H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.86 (d, *J* = 10.8 Hz, 1H), 4.73 (s, 2H), 4.64 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 10.8 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 4.33 (m, 1H, H-5), 4.27 (s, 1H, H-2), 3.96 (t, *J* = 9.2 Hz, 1H, H-4), 3.89 (dd, *J* = 2.9, 9.1 Hz, 1H, H-3), 3.83 (dd, *J* = 4.5, 10.8 Hz, 1H, H-6), 3.70 (dd, *J* = 1.4, 10.8 Hz, 1H, H-6'), 2.71 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.4, 138.39, 137.8, 134.0, 131.8 (2 carbons), 129.2 (2 carbons), 128.8 (2 carbons), 128.6 (2 carbons), 128.5 (2 carbons) 128.3, 128.2 (2 carbons), 128.1 (3 carbons), 128.9 (2 carbons), 127.9, 127.7, 127.6, 87.5, 80.5, 75.4, 74.7, 73.6, 72.4, 72.3, 70.1, 69.0.

Methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (13).[101] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.3 - 7.2 (m, 15H), 7.19 (dd, J = 7.5, 1.9 Hz, 3H), 4.83 (d, J = 11.1 Hz, 1H), 4.81 (d, J = 1.4 Hz, 1H, H-1), 4.69 (d, J = 12.2 Hz, 2H), 4.66 (d, J = 12.5 Hz, 1H), 4.55 (d, J = 12.5 Hz, 1H), 4.52 (d, J = 11.1 Hz, 1H), 4.03 (d, J = 1.9 Hz, 1H), 3.86 (m, 2H), 3.74 (m, 3H), 3.38 (s, 3H, OMe).

Phenyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (16). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 - 7.3 (m, 20H), 5.61 (s, 1H, H-1), 5.03 (d, *J* = 10.9 Hz, 1H), 4.8 - 4.7 (m,

5H), 4.2 - 4.1 (m, 2H), 4.08 (broad, 1H), 3.91 (dd, *J* = 2.9, 8.9 Hz, 1H, H-3), 3.90 (s, 2H) 2.13 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.6, 138.4, 1381, 134.2, 132.1, 129.4, 128.7, 128.3, 128.2, 128.1, 128.0, 127.9, 86.3, 80.4, 76.7, 75.6, 75.0, 73.6, 72.6, 72.5, 62.4; ESI/APCI Calcd for $C_{33}H_{34}N_3O_5SNa$ ($[M+Na]^+$) m/z 565.2025; measured m/z 565.2026.

Phenyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (17).[103] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 - 7.2 (m, 20H), 5.61 (s, 1H, H-1), 5.00 (d, *J* = 10, 8 Hz, 1H), 4.76 (d, *J* = 12.3 Hz, 1H), 4.7-4.6 (m, 4H), 4.4 (m, 3H), 4.0 (m, 2H), 3.93 (dd, *J* = 2.62, 9.1 Hz, 1H, H-3), 2.06 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 138.2, 138.1, 137.9, 134.1, 131.8129.1, 128.6, 128.5, 128.2, 127.9, 127.9127.7, 85.6, 80.2, 76.1, 75.4, 74.7, 72.2 72.0, 71.0, 63.6, 20.9.

Phenyl 2,3,4-tri-*O*-benzyl-6-deoxy-1-thio-α-D-mannopyranoside (20). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.6 - 7.4 (m, 20 H), 5.63 (d, *J* = 1.41 Hz, 1H, H-1), 5.09 (d, *J* =10.8 Hz, 1H), 4.9 - 4.7 (m 5H), 4.3 (m, 1H, H-5), 4.12 (dd, *J* = 1.7, 2.9 Hz, 1H, H-2), 3.98 (dd, *J* = 3.0, 9.3 Hz, 1H, H-3), 3.83 (t, *J* = 9.3 Hz, 1H, H-4), 1.48 (d, *J* = 6.2 Hz. 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.9, 138.6, 138.2, 135.0, 131.6, 129.3, 128.7, 128.3, 128.1, 128.0, 127.6, 86.1, 80.8, 80.4, 76.9, 75.8, 72.5, 72.4, 69.7, 18.3; ESI/APCI Calcd for $C_{33}H_{34}O_4SNa$ ($[M+Na]^+$) m/z 549.2076; measured m/z 549.2083.

2,3,4-tri-*O*-benzyl-6-deoxy-α-D-mannopyranoside (21).[131] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.4 (m, 15H), 5.16 (s, broad, 1H), 4.96 (d, *J* = 10.6 Hz, 1H), 4.6 – 4.8 (m, 6H), 3.9 (m, 2H), 3.8 (m, 1H), 3.6 (m, 1H), 3.4 (m, 1H), 2.91 (d, *J* = 3.4 Hz, 1H), 1.33 (d, *J* = 6.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.68, 138.65, 138.4,

138.3, 138.1, 128.7, 128.6, 128.5, 128.47 (4 carbons), 128.4, 128.2, 128.1 (2 carbons), 128.07 (2 carbons), 127.98, 127.92, 127.8 (2 carbons), 127.74 (2 carbons), 127.6, 93.4 (β), 93.0, 83.1, 80.6, 80.0, 79.7, 76.6, 75.5, 75.4, 75.1, 74.9, 72.9 (2 carbons), 72.3, 71.7, 68.3, 18.2, 18.0.

Acetyl 2,3,4-tri-O-benzyl-6-deoxy-α-D-mannopyranoside (22).[132] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.5 (m, 15H), 6.13 (d, *J* = 2.1 Hz, 1H, H-1), 5.57 (d, *J* = 0.7 Hz, H-1B), 4.98 (d, *J* = 11.0 Hz, 1H, β), 4.97 (d, *J* = 10.7 Hz, 1H), 4.89 (s, 1H), 4.79 (d, *J* = 12.4Hz, 1H), 4.75 (d, *J* = 12.4Hz, 1H), 4.68 (d, *J* = 11.0Hz, 1H, β), 4.67 (d, *J* = 10.6Hz, 1H), 4.63 (d, *J* = 2.4Hz, β), 4.62 (d, *J* = 11.8 Hz, 1H), 4.57 (d, *J* = 11.8 Hz, 1H), 3.94 (d, *J* = 2.1 Hz, 1H), 3.7 – 3.9 (m, 3H), 3.6 – 3.8 (m, 4H), 3.47 (m, 1H), 2.09 (s, CH_3 for β), 2.03 (s, 3H, CH_3), 1.39 (d, *J* = 6.2Hz, CH_3 for β), 1.36 (d, *J* = 6.2 Hz, 3H, CH_3) ; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.2, 138.4, 138.37 (2 carbons β), 138.3, 138.1 (β), 137.9, 128.6, 128.5, 128.2, 128.19, 127.96, 127.90, 127.8, 127.7, 93.1, 91.8, 82,4, 79.9, 79.8, 79.3, 75.7, 75.6, 74.3, 73.7, 72.9, 72.6, 72.3, 72.2, 70.6, 21.1, 18.2, 18.0.

Phenyl 6-azido-2,3,4-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (23). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.6 - 7.3 (m, 20H), 5.75 (d, *J* = 1.5 Hz, 1H, H-1), 5.13 (d, *J* = 11.0 Hz, 1H), 4.9 - 4.7 (m, 5H), 4.4 (m, 1H, H-5), 4.2 (m, 2H), 4.04 (dd, *J* = 2.9, 9.2 Hz, 1H, H-6), 3.6 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.6, 138.4, 138.2, 134.4, 131.8, 131.8, 129.5, 128.8, 128.4, 128.4, 128.3, 128.2, 127.9, 86.1, 80.4, 76.5, 75.8, 75.7, 72.9, 72.4, 72.3, 51.8; ESI/APCI Calcd for $C_{33}H_{33}N_3O_4SNa$ ($[M+Na]^+$) m/z 590.2089; measured m/z 590.2087.

Phenyl 2,3,4-tri-*O*-benzyl-6-fluoro-1-thio-α-D-mannopyranoside (24). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 -7.3 (m, 20H), 5.68 (d, *J* = 1.2 Hz, 1H, H-1), 5.06 (d, *J* = 10,7 Hz, 1H), 4.9 - 4.6 (m, 7H), 4.4 (m, 1H, H-5), 4.17 (t, *J* = 9.4 Hz, 1H, H-4), 4.10 (dd, *J* = 1.7, 4.4 Hz, 1H, H-2), 3.97 (dd, *J* = 2.9, 9.2 Hz, 1H, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.5, 138.3, 138.1, 134.5, 131.6, 129.4, 128.8, 128.7, 128.3, 128.2, 128.1, 127.8, 86.1, 83.3, 81.6, 80.4, 76.4, 75.6, 74.1, 74.0, 72.6, 72.4; ESI/APCI Calcd for $C_{33}H_{33}O_4FSNa$ ($[M+Na]^+$) m/z 567.1981; measured m/z 567.1980.

Phenyl 2,3-di-*O*-acetyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (29). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.3 -7.5 (m, 10H), 5.63 (dd, *J* = 1.3, 3.4 Hz, H-2, 1H,), 5.61(s, 1H, H-1'), 5.45 (d, *J* = 0.8 Hz, H-1, 1H,), 5.43 (dd, *J* = 3.4, 10.5 Hz, H-3, 1H), 4.5 (m, 1H, H-5), 4.27 (dd, *J* = 4.9 Hz, 10.4 Hz, H-6, 1H,), 4.15 (t, *J* = 9.7 Hz, H-4, 1H), 3.89 (t, *J* = 10.3 Hz, H-6', 1H), 2.18 (s, 3H, CH_3), 2.06 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.9, 169.8, 137.1, 132.2 (2 carbons), 129.3 (3 carbons), 128.4 (3 carbons), 128.2, 126.3 (2 carbons), 102.1, 86.9, 76.3, 71.6, 68.6, 68.5, 65.3, 21.0, 20.9; ESI/APCI Calcd for $C_{23}H_{24}O_7SNa$ ($[M+Na]^+$) m/z 467.1140; measured m/z 467.1141.

Phenyl 2-*O*-benzyl-4,6-benzylidene-1-thio-α-D-mannopyranoside (30).[133] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (m, 2H), 7.3 – 7.5 (m, 13H), 5.60 (s, 2H,), 4.77 (d, *J* = 11.6 Hz, 1H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.32 (m, 1H), 4.25 (m, 1H), 4.15(m, 2H), 4.02 (t, *J* = 6.8 Hz, 1H), 3.85 (t, *J* = 10.1 Hz, 1H) 2.47 (d, *J* = 7.9 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.4, (2 carbons), 133.8, 132.0 (2 carbons), 129.4 (3 carbons), 128.9 (2 carbons), 128.5 (2 carbons), 128.4, 128.3 (2 carbons), 127.9, 126.5 (2 carbons), 102.4, 86.4, 80.2, 79.8, 73.4, 69.2, 68.7, 64.9.

Phenyl 3-*O*-benzyl-4,6-benzylidene-1-thio-α-D-mannopyranoside (31).[134] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 – 7.5 (m, 15H), 5.64 (s, 1H), 5.61 (s, 1H, H-1), 4.92 (d, *J* = 11.7 Hz, 1H), 4.76 (d, *J* = 11.7 Hz, 1H), 4.3 (m, 2H), 4.2 (m, 2H), 3.99 (dd, *J* = 3.1, 9.5 Hz, 1H), 3.89 (t, *J* = 10.2 Hz, 1H), 2.87 (s, 1H, OH).

Phenyl 3-*O*-acetyl-2-*O*-benzyl-4,6-benzylidene-1-thio-α-D-mannopyranoside (32). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48 (m, 4H), 7.3 – 7.4 (m, 11H), 5.61 (s, 1H), 5.58 (d, *J* = 1.3 Hz, 1H, H-1), 5.32 (dd, *J* = 3.4, 10.4 Hz, 1H, H-3), 4.71 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.4 (m, 1H, H-5), 4.27 (m, 3H), 3.90 (t, *J* = 10.2 Hz, 1H, H-4), 2.06 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 133.8, 132.0, (2 carbons) 129.4, (2 carbons), 129.3, 128.8, (2 carbons), 128.5 (2 carbons), 128.36, 128.31 (2 carbons), 127.9, 126.5 (2 carbons), 102.1, 86.6, 77.8, 76.4, 73.3, 70.7, 68.7, 65.5, 21.2; ESI/APCI Calcd for $C_{28}H_{28}O_6SNa$ ($[M+Na]^+$) m/z 515.1504; measured m/z 515.1517.

Phenyl-3-*O*-benzoyl-2-*O*-benzyl-4,6-benzylidene-1-thio-α-D-mannopyranoside (33). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H), 7.1 – 7.6 (m, 18H) 5.67 (s, 1H, H-1′), 5.61 (s, 1H, H-1), 5.59 (dd, *J* = 3.0, 9.7 Hz, 1H, H-3), 4.70 (d, *J* = 11.9 Hz, 1H), 4.57 (d, *J* = 11.9 Hz, 1H), 4.48 (m, 2H), 4.40 (d, *J* = 3.0 Hz, 1H), 4.30 (dd, *J* = 4.2, 10.1 Hz, 1H, H-2), 3.97 (t, *J* = 9.7 Hz, 1H, H-4); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 137.5, 137.4, 133.9, 133.4, 132.0 (2 carbons), 130.1, 130.05, 129.4 (2 carbons), 129.2, 128.65 (2 carbons), 128.61 (3 carbons), 128.4 (2 carbons), 128.2 (2 carbons), 127.9, 126.4 (2 carbons), 101.9, 86.8, 79.1, 76.6, 73.4, 71.4, 68.8, 65.6; ESI/APCI Calcd for $C_{33}H_{30}O_6SNa$ ($[M+Na]^+$) m/z 577.1661; measured m/z 577.1667.

Phenyl-6-*O*-acetyl-3-*O*-benzoyl-2,6-di-*O*-benzyl-1-thio-α-D-mannopyranoside (34). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.08 (m, 2H), 7.65 – 7.16 (m, 38H), 5.63 (s, 1H, H-1), 5.50 (dd, *J* = 3.2, 9.3 Hz, 1H, H-3), 4.79 (d, *J* = 10.8 Hz, 1H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.61 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.48 (m, 1H, H-5), 4.27 (m, 1H, H-2),; 4.19 (t, *J* = 9.5 Hz, 1H, H-4), 2.07 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 165.7, 137.6, 137.5, 134.0, 133.5, 132.0, 130.1,; 130.0, 129.9, 128.7, 128.6, 128.5, 18.2, 128.2, 128.0, 127.9, 127.8, 85.6, 75.2, 74.7, 73.8, 73.7, 72.6, 70.9, 63.6, 21.1; ESI/APCI Calcd for $C_{35}H_{34}O_7SNa$ ($[M+Na]^+$) m/z 621.1923; measured m/z 621.1926.

Phenyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside (37).[106] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49 (m, 2H), 7.2 – 7.4 (m, 13H), 5.56 (d, *J* = 1.9 Hz, 1H, H-1) 5.23 (dd, *J* = 3.3, 9.3 Hz, 1H, H -3), 4.74 (d, *J* = 11.2Hz, 1H), 4.69 (d, *J* = 12.2 Hz, 1H), 4.60 (d, *J* = 11.2 Hz, 1H), 4.51 (d, *J* = 12.2 Hz, 1H), 4.4 (m, 1H, H-5), 4.3 (m, 2H), 4.14 (dd, *J* = 2.0, 3.2 Hz, 1H, H-2), 4.00 (t, *J* = 9.4 Hz, 1H, H-4), 2.05 (s, 3H, CH_3), 2.01 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 170.2, 137.9, 137.7, 133.9, 132.0, (2 carbons), 129.2, (2 carbons), 128.7, (2 carbons), 128.6 (2 carbons), 128.2, 128.17, 128.07 (2 carbons), 127.9 (2 carbons), 127.8, 85.3, 77.4, 77.1, 75.2, 74.0, 73.7, 72.5, 70.8, 63.5, 21.2, 21.1.

Phenyl 2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-1-thio-α-D-mannopyranoside (38). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 – 7.5 (m, 15H), 5.62 (dd, *J* = 1.6, 3.1 Hz, 1H, H-2), 5.50 (d, *J* = 1.4 Hz, 1H, H-1), 4.96 (d, *J* = 10.7 Hz, 1H), 4.75 (d, *J* = 11.0 Hz, 1H), 4.6 – 6.7 (m, 2H), 4.3 – 4.5 (m, 3H, H-5, H-6, H-6′), 4.0 (m, 1H, H-3), 3.81 (t, *J* = 9.4 Hz, 1H, H-4), 2.17 (s, 3H, CH_3), 2.04 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 170.4,

138.1, 137.6, 133.4, 132.2 (2 carbons), 129.3 (3 carbons), 128.7 (2 carbons), 128.7 (2 carbons), 128.5, 128.4 (2 carbons), 128.3 (2 carbons), 128.2, 128.1 (2 carbons), 86.3, 78.6, 75.5, 74.5, 72.1, 70.9, 70.2, 63.5, 21.2, 21.0; ESI/APCI Calcd for $C_{30}H_{32}O_7NaS$ ($[M+Na]^+$) m/z 559.1766; measured m/z 559.1768.

Acetyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (42).[107] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4 - 7.2 (m, 15H), 6.18 (d, *J* = 2.1 Hz, 1H, H-1), 4.95 (d, *J* = 10.6 Hz, 1H), 4.77 (d, *J* = 12.4 Hz, 1H), 4.72 (d, *J* = 12.4Hz, 1H), 4.6 (m, 3H), 4.3 (m, 2H, H-6, H-6'), 4.0 – 3.8 (m, 2H, H-2, H-5), 3.73 (t, *J* = 2.5Hz, 5.2 Hz, 1H), 2.06 (s, 3H, CH3), 2.03 (s, 3H, CH3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 168.9, 138.0 (2 carbons), 137.8, 128.6 (2 carbons), 128.52 (2 carbons), 128.50 (2 carbons), 128.3 (2 carbons), 128.0 (3 carbons), 127.9, (2 carbons), 127.8 (2 carbons), 91.6, 79.2, 75.5, 73.9, 73.2, 72.4 (2 carbons), 72.1, 63.2, 21.1, 20.9.

Acetyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (43).[135] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4 - 7.1 (m, 20H), 6.23 (d, *J* = 2.1 Hz, 1H, H-1) 4.90 (d, *J* = 10, 6 Hz, 1H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.73 (d, *J* = 12.4 Hz, 1H), 4.67 (d, *J* = 12.1 Hz, 1H) 4.59 (d, *J* = 11.7 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 10.6 Hz, 1H), 4.54 (d, *J* = 12.1 Hz, 1H), 4.09 (t, *J* = 9.6 Hz, H-4), 3.9 - 3.7 (m, 5H), 2.02 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 169.1, 138.3, (2 carbons), 138.2, 137.9, 128.5 (6 carbons), 128.4 (2 carbons), 128.16 (2 carbons), 128.11 (2 carbons), 127.9 (2 carbons), 127.8 (4 carbons), 127.6, 91.9, 79.2, 75.4, 74.5, 74.3, 73.6, 73.4, 72.5, 72.2, 69.0, 21.1.

Acetyl 3,6-di-*O*-acetyl-2,4-tri-*O*-benzyl-α-D-mannopyranoside (44).[136] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 – 7.3 (m, 10H), 6.19 (d, *J* = 2.1 Hz, 1H, H-1), 5.22 (dd, *J*

= 3.3, 9.0 Hz, 1H, H-3), 4.73 (d, *J* = 12.1, 1H), 4.71 (d, *J* = 11.2 Hz, 1H), 4.60 (d, *J* = 11.2 Hz, 1H), 4.57 (d, *J* = 12.1 Hz, 1H), 4.34 (dd, *J* = 2.2, H-6), 4.31 (dd, *J* = 4.4 Hz, H-6'), 4.00 (t, *J* = 9.2 Hz, 1H, H-4), 3.95 (m, 1H, H-5), 3.87(dd, *J* = 2.3, 3.3 Hz, H-2), 2.12 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 1.99 (s, 3H, CH_3) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 170.3, 169.1, 137.8, 137.6, 128.7, 128.6 (2 carbons), 128.2 (2 carbons), 128.1 (2 carbons), 128.0 (2 carbons), 91.4, 77.4, 75.2, 74.6, 73.4, 72.9 (2 carbons), 72.3, 63.2, 21.2, 21.1, 21.0.

Acetyl 4,6-di-*O*-acetyl-2,3-tri-*O*-benzyl-α-D-mannopyranoside (45). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 10H), 6.18 (d, *J* = 1.7 Hz, 1H), 5.50 (t, *J* = 9.9 Hz, 1H, H-4), 4.73 (s, 2H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.22 (dd, *J* = 5.1, 12.4 Hz, 1H, H-6), 4.12 (dd, *J* = 2.4, 12.4 hz, 1H, H-6′) 3.92 (m, 1H, H-5), 3.7 – 3.8 (m, 2H), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.03 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1, 169.8, 168.9, 137.9, 137.8, 128.62, 128.60, 128.2, 128.0, 127.7, 91.9, 76.2, 73.0, 72.8, 72.0, 71.6, 67.6, 62.8, 21.2, 21.1, 21.0; ESI/APCI Calcd for $C_{26}H_{30}O_9Na$ ($[M+Na]^+$) m/z 509.1788; measured m/z 509.1781.

Methyl 2-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (47).[108] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (m, 2H), 7.3 (m, 8H), 5.59 (s, 1H, H-1′), 4.78 (d, *J* = 11.7 Hz, 1H), 4.76 (s, 1H, H-1), 4.70 (d, *J* = 11.7 Hz, 1H), 4.28 (dd, *J* = 3.9, 9.3 Hz, 1H), 4.08 (dd, *J* = 3.6, 6.2 Hz, 1H), 3.92 (t, *J* = 9.1 Hz, 1H), 3.7 – 3.8 (m, 3H), 3.38 (s, 3H, OMe), 2.20 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.8, 137.5, 129.3, 128.8 (2 carbons), 128.5 (2 carbons), 128.3, 128.2 (2 carbons), 126.5 (2 carbons), 102.4, 99.6, 79.7, 78.7, 77.4, 73.9, 69.0, 68.9, 63.5, 55.2.

Methyl 3-*O*-acetyl-2-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (49).[137] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47 (m, 2H), 7.35 (m, 8H), 5.59 (s, 1H), 5.28 (dd, *J* = 3.4, 10.5 Hz, 1H, H-3), 4.74 (d, *J* = 1.6 Hz, 1H, H-1), 4.68 (d, *J* = 11.9 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 1H), 4.3 (m, 1H), 4.2 (m, 1H), 3.98 (dd, *J* = 1.6, 3.4 Hz, 1H), 3.89 (m, 2H), 3.39 (s, 3H, OMe), 2.04 (s, 3H, CH_3).

Methyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (50).[138] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.3 – 7.6 (m, 10 H); 4.90 (d, *J* = 11.0 Hz,1H), 4.75 (d, *J* = 1.4 Hz, 1H, H-1), 4.72 (d, *J* = 11.7 Hz, 1H), 4.66 (d, *J* = 11.0 Hz, 1H), 4.59 (d, *J* = 11.7 Hz, 1H), 3.98 (m, 1H, H-5), 3.86 (dd, *J* = 2.7, 11.7 Hz, 1H, H-6), 3.77(dd, *J* = 4.1, 11.7 Hz, 1H), 3.72(dd, *J* = 1.5, 3.8 Hz, 1H, H-3); 3.67 (t, *J* = 9.6 Hz, 1H, H-4), 3.63 (dd, *J* = 2.4, 3.8 Hz, 1H, H-2); 3.33 (s, 3H, OMe).

Methyl 2-*O*-acetyl-3-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (52).[139] ^{1}H NMR ($CDCl_3$, 400 MHz) δ7.5 (m, 2H), 7.2 – 7.4 (m, 8H), 5.64 (s, 1H, H-1′), 5.41 (dd, *J* = 1.5, 3.2 Hz, 1H, H-2), 4.69 (m, 3H), 4.29 (m, 1H), 4.06 (m, 1H), 4.02 (m, 1H), 3.8 (m, 2H), 3.38 (s, 3H, OMe), 2.17 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 138.2, 137.7, 129.1, 128.6 (2 carbons), 128.4 (2 carbons), 127.9 (3 carbons), 126.3 (2 carbons), 101.8, 100.0, 78.5, 74.0, 72.3, 69.8, 68.9, 63.9, 55.3, 21.2.

Methyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-mannopyranoside (53). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.3 (m, 10H), 5.24 (dd, *J* = 3.3, 9.2 Hz, 1H, H-3), 4.74 (d, *J* = 1.8 Hz, 1H, H-1), 4.70 (d, *J* = 11.2 Hz, 1H), 4.67 (d, *J* = 12.2 Hz, 1H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.57 (d, *J* = 12.2 Hz, 1H), 4.35 (m, 2H), 3.92 (t, *J* = 9.4 Hz, 1H, H-4), 3.88 (dd, *J* = 2.1, 3.2 Hz, 1H, H-2), 3.85 (m, 1H, H-5), 3.38 (s, 3H, OCH_3), 2.08 (s, 3H, CH_3), 1.98 (s,

3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 170.3, 138.1, (2 carbons), 128.65 (2 carbons), 128.61, 128.6 (2 carbons), 128.0 (2 carbons), 127.9 (3 carbons), 98.9, 77.3, 76.0, 74.9, 74.1, 73.6, 73.1, 69.9, 63.6, 55.1, 21.2, 21.0; ESI/APCI Calcd for $C_{25}H_{34}O_8$ ($[M+NH_4]^+$) m/z 476.2350.

Methyl 2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (54).[140] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.2 - 7.3 (m, 10H), 5.3 (dd, *J* = 1.7, 3.4 Hz, 1H, H-2), 4.90 (d, *J* = 10.6 Hz, 1H), 4.70 (d, *J* = 1.7 Hz, 1H, H-1), 4.69 (d, *J* = 10.9 Hz, 1H), 4.54 (d, *J* = 10.6 Hz, 1H), 4.52 (d, *J* = 10.9 Hz, 1H), 4.33 (m, 2H), 3.98 (dd, *J* = 3.4, 8.9 Hz, 1H, H-3), 3.82 (m, 1H, H-5), 3.73(t, *J* = 9.6 Hz, 1H, H-4), 3.35 (s, 3H, OMe), 2.15 (s, 3H), 2.05 (s, 3H).

6'-Azidohexyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (55). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.6 (m, 30H), 5.0 - 4.9 (m, 3H), 4.88 (d, *J* = 1.7 Hz, 1H), 4.80 (d, *J* = 12.4 Hz, 1H), 4.74 (d, *J* = 12.4 Hz, 1H), 4.6 - 4.7 (m, 4H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.4 (m, 1H), 4.3 – 4.4 (m, 3H), 3.9 – 4.0 (m, 6H), 3.8 – 3.9 (m, 3H), 3.6 (m, 1H), 3.4 – 3.6 (m, 3H), 3.27 (t, *J* = 6.9 Hz, 4H), 2.09 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 1.6 (m, 8H), 1.3 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.05 (β), 171.0 (α), 138.8, 138.5 (2 carbons), 138.4 (2 carbons), 138.29 (2 carbons), 138.28, 137.16, 128.6 (3 carbons), 128.5 (4 carbons), 128.47 (3 carbons), 128.33 (2 carbons), 128.28, 128.23, 127.9 (2 carbons), 127.89 (3 carbons), 127.79 (5 carbons), 127.78 (2 carbons), 127.6, 101.9 (β), 98.0 (α), 82.4, 80.3, 75.3, 74.8, 74.7, 74.68, 73.9, 73.8, 73.6, 72.7, 72.2, 71.5, 70.2, 69.9, 67.7, 63.9, 63.7, 51.4, 29.6, 29.4, 28.9, 28.87,

26.6, 25.9, 25.83, 21.06, 21.04; ESI/APCI Calcd for $C_{35}H_{43}N_3O_7Na$ ($[M+Na]^+$) m/z 640.2999; measured m/z 640.2998.

6'-Azidohexyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (56). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.5 (m, 15H), 4.98 (d, *J* = 12.4 Hz, (β)), 4.96 (d, *J* = 10.9 Hz, (β)), 4.95 (d, *J* = 10.7 Hz, 1H), 4.87 (d, *J* = 12.5 Hz, (β)), 4.8 (m, 2H), 4.6 – 4.72 (m, 4H), 4.55 (d, *J* = 12.0 Hz, (β)), 4.48 (d, *J* = 12.0 Hz, (β)), 3.9 – 4.0 (m, 4H), 3.7 – 3.83 (m, 3 H), 3.6 (m, 2H), 3.2 – 3.4 (m, 3H), 2.04 (s, 1H, OH), 1.5 (m, 4H), 1.3 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 138.6, 138.4 (2 carbons), 138.3, 138.2, 128.55 (2 carbons), 128.5 (3 carbons), 128.2 (2 carbons), 127.9 (3 carbons), 127.8, 127.7 (2 carbons), 127.6, 101.8 (β), 98.3, 82.4 (β), 80.4, 75.9 (β), 75.4, 75.1, 75.0, 74.1 (β), 73.9 (β), 73.0, 72.3, 72.2, 71.6 (β), 70.0 (β), 67.5, 62.5, 51.5, 29.6 (β), 29.3, 28.9 (β), 28.8, 26.6, 25.8; ESI/APCI Calcd for $C_{33}H_{41}N_3O_6Na$ ($[M+Na]^+$) m/z 598.2893; measured m/z 598.2907.

6'-Azidohexyl 3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-mannopyranoside (57). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.3 (m, 10H), 5.25 (dd, *J* = 3.3, 9.1 Hz, 1H, H-3), 4.82 (s, 1H, H-1), 4.70 (d, *J* = 11.2 Hz, 1H), 4.66 (d, *J* = 12.3 Hz, 1H), 4.60 (s, 1H), 4.58 (d, *J* = 11.1 Hz, 1H), 4.3 (m, 2H, H-6, H-6'), 3.9 (t, *J* = 9.6 Hz, 1H, H-4), 3.9 (m, 2H, H-2, H-5), 3.7 (m, 1H), 3.4 (m, 1H), 3.27 (t, *J* = 6.9 Hz, 2H), 2.08 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 170.3, 138.1, 138.0, 128.7 (2 carbons), 128.6 (2 carbons), 128.1 (2 carbons), 128.0 (2 carbons), 127.9 (2 carbons), 97.9, 76.2, 75.0, 74.1, 73.6, 73.1, 69.9, 68.0, 63.6, 57.6, 29.4, 28.9, 26.7, 26.6, 21.3, 21.1; ESI/APCI Calcd for $C_{30}H_{39}N_3O_8Na$ ($[M+Na]^+$) m/z 592.2635; measured m/z 592.2629.

6'-Azidohexyl 2,4-di-*O*-benzyl-α-D-mannopyranoside (58). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.4 (m, 10H), 4.90 (d, *J* = 11.0 Hz, 1H), 4.83 (d, *J* = 1.4 Hz, 1H, H-1), 4.73 (d, *J* = 11.7 Hz, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 4.60 (d, *J* = 11.0 Hz, 1H), 4.0 (m, 1H), 3.8 (m, 2H), 3.72 (dd, *J* = 1.4, 3.8 Hz, 1H, H-2), 3.6 – 3.7 (m, 3H), 3.3 (m, 1H), 3.25 (t, *J* = 6.9 Hz, 2H), 2.34 (d, *J* = 9.3 Hz, 1H, OH), 2.05 (s, broad, 1H, OH), 1.56 (m, 4H), 1.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.4, 137.8, 128.7 (2 carbons), 128.6 (2 carbons), 128.2 (3 carbons), 127.9 (3 carbons), 97.1, 78.6, 76.6, 75.1, 73.2, 71.9, 71.4, 67.6, 62.4, 51.4, 29.3, 28.8, 26.6, 25.8; ESI/APCI Calcd for $C_{26}H_{35}N_3O_6Na$ ($[M+Na]^+$) m/z 508.2424; measured m/z 508.2438.

6'-Azidohexyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (59). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.1 – 7.5 (m, 15H), 5.37 (dd, *J* = 3.0, 1.6 Hz, 1H), 4.87 (d, *J* = 12.2 Hz, 1H), 4.84 (d, *J* = 1.6 Hz, 1H), 4.72 (d, *J* = 11.2 Hz, 1H), 4.69 (d, *J* = 12.2 Hz, 1H), 4.55 (d, *J* = 10.7 Hz, 1H), 4.52 (d, *J* = 11.2 Hz, 1H), 4.48 (d, *J* = 10.7 Hz, 1H), 4.00 (dd, *J* = 8.9, 3.0 Hz, 1H), 3.89 (dd, *J* = 9.2, 9.2 Hz, 1H), 3.6 – 3.8 (m, 2H), 3.52 (dd, *J* = 6.8, 6.8 Hz, 1H), 3.43 (dd, *J* = 6.8, 6.3 Hz, 1H), 3.40 (dd, *J* = 6.8, 6.3 Hz, 1H), 3.25 (t, *J* = 6.8 Hz, 2H), 2.16 (s, 3H), 1.5 – 1.6 (m, 4H), 1.3 – 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 170.6, 138.6, 138.49, 138.22, 128.7, 128.58 (2 carbons), 128.53 (3 carbons), 128.25 (2 carbons), 128.14 (2 carbons), 127.96 (2 carbons), 127.93, 127.85, 127.78, 97.9, 78.4, 75.3, 74.5, 73.5, 71.9, 71.5, 69.03, 68.97, 67.8, 51.5, 29.3, 28.8, 26.6, 25.8, 21.2; HRFAB Calcd for $C_{35}H_{43}N_3O_7Na$ ($[M+Na]^+$) m/z 640.2999; measured m/z 640.2987.

6'-Azidohexyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (60). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 – 7.3 (m, 15H), 4.90 (d, *J* = 1.5 Hz, 1H, H-1), 4.82 (d, *J* = 10.7

Hz, 1H), 4.72 (d, *J* = 11.6 Hz, 1H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.50 (d, *J* = 10.7 hz, 1H), 4.04 (m, 1H), 3.87 (m, 2H), 3.65 – 3.8 (m, 4H), 3.41 (m, 1H), 3.25 (t, *J* = 6.9 hz, 2H), 1.58 (m, 4H), 1.36 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.4 (2 carbons), 138.1, 128.7 (2 carbons), 128.6 (2 carbons), 128.5 (3 carbons), 128.2 (3 carbons), 128.12, 128.06 (4 carbons), 128.04 (2 carbons), 127.8, 127.7, 99.3, 80.5, 77.4 (3 carbons), 75.4, 74.5, 73.6, 72.2, 71.2, 69.1, 68.6, 67.751.6, 29.5, 28.9, 26.7, 25.9, ESI/APCI Calcd for $C_{33}H_{41}N_3O_6Na$ ($[M+Na]^+$) m/z 598.2884; measured m/z 598.2893.

6'-Azidohexyl-3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-manno-pyranoside (61). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 – 7.5 (m, 2H), 7.3 – 7.4 (m, 8H), 5.59 (s, 1H, H-1'), 5.31 (dd, *J* = 3.4, 10.4 Hz, 1H, H-3), 4.81 (s, 1H, H-1), 4.68 (d, *J* = 11.9 Hz, 1H), 4.64 (d, *J* = 11.9 Hz, 1H), 4.26 (d, *J* = 5.6 Hz, 1H), 4.2 (m, 1H, H-5), 3.96 (s, 1H), 3.9 (m, 2H), 3.7 (m, 1H), 3.4 (m, 1H), 3.29 (t, *J* = 6.8 Hz, 2H), 2.05 (s, 3H, CH_3), 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 137.8, 137.5, 129.2, 128.7 (2 carbons), 128.4 (2 carbons), 128.2 (2 carbons), 126.4 (2 carbons), 101.9, 99.0, 77.4, 76.6, 76.5, 73.9, 70.8, 69.0, 68.0, 64.2, 51.6, 29.4, 28.9, 26.7, 25.9, 21.3; HRFAB Calcd for $C_{28}H_{35}N_3O_7Na$ ($[M+Na]^+$) m/z 548.2373; measured m/z 548.2371.

6'-Azidohexyl-2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-D-mannopyranoside (62). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4 – 7.5 (m, 2H), 7.3 – 7.4 (m, 3H), 5.58 (s, 1H), 5.40 (dd, *J* = 3.6, 9.6 Hz, 1H, H-3), 5.33 (dd, *J* = 1.7, 3.6 Hz, 1H, H-2), 4.75 (d, *J* = 1.3 Hz, 1H, H-1), 4.27 (dd, *J* = 4.1, 9.9 Hz, 1H), 4.03 (t, *J* = 9.3 Hz, 1H), 3.9 (m, 1H, H-5), 3.85 (t, *J* = 9.9 Hz, 1H), 3.7 (m, 1H), 3.4 (m, 1H), 3.28 (t, *J* = 6.9 Hz, 2H), 2.17 (s, 3H, CH_3),

2.02 (s, 3H, CH_3), 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.0, 169.9, 137.2, 129.2, 128.4 (2 carbons), 126.2 (2 carbons), 101.9, 98.7, 77.3, 76.3, 70.3, 68.8, 68.2, 63.9, 51.5, 29.3, 28.8, 26.6, 25.8, 21.0, 20.9; HRFAB Calcd for $C_{23}H_{31}N_3O_8Na$ ($[M+Na]^+$) m/z 500.2009; measured m/z 500.2008.

6'-Azidohexyl-2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (63). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.5 - 7.6 (m, 4H), 7.2 – 7.5 (m, 26H), 5.68 (s, 1H), 5.66 (s, 1H), 5.03 (d, *J* = 12.4 Hz, 1H), 4.8 – 5.0 (m, 3H), 4.82 (d, *J* = 1.4 Hz, 1H, H-1), 4.79 (s, 1H), 4.6 – 4.7 (m, 4H), 4.47 (s, 1H), 4.2 - 4.4 (m, 3H), 4.10 (t, *J* = 6.9 Hz, 1H), 3.9 – 4.1 (m, 3H), 3.8 – 3.9 (m, 3H), 3.6 (m, 1H), 3.5 (m, 1H), 3.4 (m, 1H), 3.3 (m, 4H), 1.6 (m, 8H), 1.4 (m, 8H); ^{13}C NMR ($CDCl_3$, 75 MHz δ 138.9, 138.6, 138.5, 138.3, 137.85, 137.83, 128.9, 128.8, 128.51 (3 carbons), 128.50 (3 carbons), 128.42 (4 carbons), 128.3, (5 carbons), 128.29 (2 carbons), 128.2 (3 carbons), 127.9 (2 carbons), 127.7, 127.6 (3 carbons), 127.2 (3 carbons), 126.2 (2 carbons), 102.4, 101.5, 99.5, 79.4, 78.8, 78.1, 76.7 (2 carbons), 75.9, 74.8, 73.7, 73.3, 72.5, 70.1, 69.0, 68.7, 67.7 (2 carbons), 64.3, 51.5 (2 carbons), 29.7, 29.3, 28.9 (2 carbons), 26.6 (2 carbons), 25.8; HRFAB Calcd for $C_{33}H_{39}N_3O_6Na$ ($[M+Na]^+$) m/z 596.2737; measured m/z 596.2731.

6'-Azidohexyl-2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranoside (64). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 10H), 5.35 (dd, *J* = 1.7, 3.4 Hz, 1H, H-2), 4.90 (d, *J* = 10.7 Hz, 1H), 4.78 (d, *J* = 1.4 Hz, 1H, H-1), 4.71 (d, *J* = 11.0 Hz, 1H), 4.54 (d, *J* = 10.7 Hz, 1H), 4.52 (d, *J* = 11.0 Hz, 1H), 4.32 (m, 2H), 4.00 (dd, *J* = 3.4, 8.9 Hz, 1H, H-3), 3.8 – 3.9 (m, 2H), 3.74 (t, *J* = 9.3 Hz, 1H, H-4), 3.65 (m, 1H), 3.4 (m, 1H), 3.26 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H, CH3), 2.06 (s, 3H, CH3), 1.6 (m, 4H), 1.35 (m, 4H); ^{13}C NMR

($CDCl_3$, 75 MHz δ 171.0, 170.6, 138.1, 137.9, 128.7 (2 carbons), 128.6 (2 carbons), 128.34 (2 carbons), 128.32 (2 carbons), 128.1, 128.0, 97.9, 78.4, 75.5, 74.3, 73.6, 71.9, 69.8, 68.8, 68.1, 63.6, 51.6, 29.4, 28.9, 26.7, 25.9, 21.3, 21.1; ESI/APCI Calcd for $C_{30}H_{39}N_3O_8Na$ ($[M+Na]^+$) m/z 592.2635; measured m/z 592.2615.

6′-Azidohexyl 2-*O*-acetyl-3-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (65). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.5 (m, 2H), 7.4 - 7.2 (m, 8H), 5.65 (s, 1H), 5.39 (dd, *J* = 1.6, 3.3Hz, 1H, H-2), 4.78 (s, 1H, H-2), 4.72 (d, *J* = 12.0Hz, 1H,), 4.68 (d, *J* = 12.0 H_Z, 1H), 4.3 (m, 1H), 4.1 - 4.0 (m, 2H), 3.9 - 3.8 (m, 2H), 3.7 (m, 1H), 3.4 (m, 1H), 3.3 (m, 2H), 2.18 (s, 3H, CH_3), 1.60 (m, 4H), 1.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.4, 138.1, 137.5, 129.0, 128.4, 128.3, 127.7, 126.1, 101.6, 98.9, 78.5, 77.3, 74.0, 72.3, 69.9, 68.8, 68.0, 63.9, 51.4, 29.3, 28.8, 26.6, 25.8, 21.1; ESI/APCI Calcd for $C_{28}H_{37}N_3O_7Na$ ($[M+Na]^+$) m/z 548.2356; measured m/z 548.2373.

6'-Azidohexyl-4,6-di-*O*-acetyl-2,3-di-*O*-benzyl-α-D-mannopyranoside (66). ^1H NMR ($CDCl_3$, 300 MHz) δ7.25 – 7.4 (m, 10H), 5.41 (t, *J* = 9.6 Hz, 1H, H-4), 4.83 (d, *J* = 1.7 Hz, 1H, H-1), 4.77 (d, *J* = 12.4 Hz, 1H), 4.67 (d, *J* = 12.4 Hz, 1H), 4.59 (d, *J* = 12.4 Hz, 1H), 4.48 (d, *J* = 12.4 Hz, 1H), 4.21 (dd, *J* = 5.5, 12.0 Hz, 1H), 4.11 (dd, *J* = 2.7, 12.0 Hz, 1H), 3.8 (m, 2H), 3.63 (m, 1H), 3.37 (m, 1H), 3.26 (t, *J* = 6.9 Hz, 2H), 2.07 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.57 (m, 4H), 1.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 169.9, 138.4 (2 carbons), 128.55 (2 carbons), 128.52 (2 carbons), 128.0 (2 carbons), 127.8 (2 carbons), 127.6 (2 carbons), 98.5, 77.4 (2 carbons), 74.4, 73.0, 72.1, 69.3, 68.4, 67.9, 63.3, 51.5, 29.4, 28.9, 26.7, 25.9, 21.1, 21.0; ESI/APCI Calcd for $C_{30}H_{39}N_3O_8Na$ ($[M+Na]^+$) m/z 592.2635; measured m/z 592.2638.

6′-Azidohexyl-3-*O*-benzoyl-2-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (67). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H,), 7.5 (m, 1H,), 7.4 - 7.2 (m, 12H), 5.65 (s, 1H, H-1'), 5.62 (1H, H-3), 4.87 (s, 1H, H-1), 4.67 (s, 2H), 4.3 - 4.2 (m, 2H), 4.1 (m, 1H), 3.9 - 3.8 (m, 2H), 3.79 (m, 1H), 3.4 (m, 1H); 3.3 (t, *J* = 6.9 Hz, 2H), 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.1, 137.8, 137.6, 134.7, 133.6, 133.3, 130.2, 130.1, 129.9, 129.1, 128.8, 128.7, 128.6, 128.4, 128.3, 128.1, 127.9, 126.3, 101.9, 99, 76.7, 76.3, 74.0, 71.5, 69.1, 67.9, 64.3, 51.6, 29.5, 29.0, 26.7, 26.0; ESI/APCI Calcd for $C_{33}H_{41}N_4O_7$ ($[M+NH_4^+]^+$) m/z 605.2975; measured m/z 605.2959.

Phenyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (68). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 (m, 2H), 7.1 – 7.4 (m, 33H), 5.67 (d, *J* = 1.6 Hz, 1H, H-1), 5.54 (dd, *J* = 1.8, 3.1 Hz, 1H, H-2'), 5.09 (d, *J* = 1.5 Hz, 1H, H-1'), 4.91 (d, *J* = 10.8 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.75 (d, *J* = 11.7 Hz, 1H), 4.71 (d, *J* = 11.7 Hz, 1H), 4.68 (d, *J* = 10.8 Hz, 1H), 4.62 (d, *J* = 11.0 Hz, 1H), 4.56 (d, *J* = 12.3 Hz, 1H), 4.49 (d, *J* = 12.6 Hz, 2H), 4.4 (m, 2H), 4.3 (m, 1H), 4.25 (t, *J* = 2.1 Hz, 1H), 3.9 – 4.0 (m, 5H), 3.8 – 3.9 (m, 2H), 3.7 – 3.8 (m, 2H), 3.60 (dd, *J* = 1.7, 10.6 Hz, 1H), 2.15 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 138.7, 138.6 (2 carbons), 138.4, 138.3, 138.2, 134.4, 131.9 (2 carbons), 129.2 (2 carbons), 128.7 (2 carbons), 128.6 (2 carbons), 128.55 (6 carbons), 128.50 (4 carbons), 128.4 (4 carbons), 128.3 (2 carbons), 128.2 (2 carbons), 128.0 (2 carbons), 127.9 (4 carbons), 127.8 (2 carbons), 127.7 (3 carbons), 127.6 (2 carbons), 99.9, 87.4, 80.2, 78.3, 77.0, 75.4, 75.3, 75.0, 74.6, 73.4 (2 carbons), 73.1, 72.4, 72.2, 72.1, 69.4, 69.0, 68.9,

21.3; ESI/APCI Calcd for $C_{62}H_{64}O_{11}SNa$ ($[M+Na]^+$) m/z 1039.4067; measured m/z 1039.4082.

Phenyl 2-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (69). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 (m, 2H), 7.2 (m, 33H), 5.60 (d, *J* = 1.5 Hz, 1H), 5.16 (d, *J* = 1.7 Hz, 1H), 4.90 (d, *J* = 10.7 Hz, 1H), 4.88 (d, *J* = 10.5 Hz, 1H), 4.72 (d, *J* = 11.2 Hz, 1H), 4.6 (m, 2H), 4.5 (m, 4H), 4.4 (m, 3H), 4.3 (m, 4H), 3.8 (m, 7H), 3.7 (m, 1H), 1.85 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 138.7, 138.6, 138.5, 138.4, 138.3, 138.1, 134.4, 131.5, 129.3, 129.0, 128.8, 128.6, 128.6, 128.5, 128.5, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 99.9, 87.4, 80.4, 79.8, 78.6, 76.5, 75.4, 75.3, 75.2, 75.0, 74.9, 74.5, 74.0, 73.5, 73.0, 72.8, 72.5, 71.0, 69.4, 63.9, 20.8; ESI/APCI Calcd for $C_{62}H_{64}O_{11}SNa$ ($[M+Na]^+$) m/z 1034.4513; measured m/z 1034.4496.

2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (70). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.1 (m, 38H), 5.56 (dd, *J* = 3.1, 1.9 Hz, 1H, H-2'), 5.26 (s, 1H, H-1'), 5.10 (s, 1H, H-1), 4.86 (d, *J* = 10.9 Hz, 2H), 4.7 - 4.6 (m, 5H), 4.6 - 4.5 (m, 6H), 4.47 (d, *J* = 10.9 Hz, 1H), 4.45 (d, *J* = 10.9 Hz, 1H), 4.0 (m, 1H), 4.0 - 3.9 (m, 4H), 3.9 (m, 1H), 3.8 - 3.7 (m, 2H), 3.7 (m, 1H), 3.7 - 3.6 (m, 2H), 2.69 (s, 1H, OH), 2.14 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 138.6, 138.5, (2 C), 138.4, 138.2, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 99.7, 93.6, 79.3, 78.9, 78.3, 75.3, 75.3, 73.1, 74.9, 74.5, 74.3, 73.6, (2 C), 72.3, 72.1, 72.0, 71.9, 69.8, 69.1 (2 C), 68.9, 21.4; ESI/APCI Calcd for $C_{56}H_{64}NO_{12}$ ($[M+NH_4]^+$) m/z 942.4429; measured m/z 942.4447.

Acetyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (71). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 30H), 6.12 (d, *J* = 2.1 Hz, 1H, H-1), 5.54 (s, 1H, H-2′), 5.14 (d, *J* = 1.4 Hz, 1H, H-1′), 4.87 (d, *J* = 10.7 Hz, 1H), 4.82 (d, *J* = 10.7 Hz, 1H), 4.6 – 4.73 (m, 5H), 4.5 – 4.6 (m, 5H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 10.7 Hz, 1H), 4.38 (d, *J* = 10.9 Hz, 1H), 3.8 – 4.0 (m, 6H), 3.6 – 3.8 (m, 4H), 2.13 (s, 3H, CH_3), 2.01 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 168.7, 138.5, 138.33, 138.32, 138.2, 138.1 (2 carbons), 128.54 (2 carbons), 128.50 (2 carbons), 128.4 (3 carbons), 128.3 (3 carbons), 128.23 (2 carbons), 128.21 (2 carbons), 127.9, 127.8 (3 carbons), 127.7, 127.68 (2 carbons), 127.6 (3 carbons), 99.5, 92.8, 79.0, 78.3, 77.3, 75.4, 75.2, 74.4, 74.2, 74.1, 73.52 (2 carbons), 73.0, 72.3, 72.1, 68.9, 68.7, 68.5, 21.2. 21.0; ESI/APCI Calcd for $C_{58}H_{62}O_{13}Na$ ($[M+Na]^+$) m/z 989.4088; measured m/z 989.4104.

Phenyl 2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-1-thio-α-D-mannopyranoside (72). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (m, 2H), 7.2 – 7.4 (m, 18H), 5.59 (s, 1H, H-1), 5.45 (dd, *J* = 1.6, 3.4 Hz, 1H, H-2′), 5.41 (dd, *J* = 3.4, 9.7 Hz, 1H, H-3′), 5.24 (t, *J* = 9.7 Hz, 1H, H-4′), 4.98 (d, *J* = 0.6 Hz, 1H, H-1′), 4.88 (d, *J* = 10.9 Hz, 1H), 4.77 (d, *J* = 11.8 Hz, 1H), 4.66 (d, *J* = 11.8 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.56 (d, *J* = 11.1 Hz, 1H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.33 (m, 1H, H-5′), 4.1 – 4.2 (m, 4H), 3.9 – 4.0 (m, 2H), 3.90 (dd, *J* = 2.6, 9.2 Hz, 1H), 3.7 – 3.8 (m, 2H), 2.14 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 1.87 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 170.05, 170.0, 169.9, 138.5, 138.4, 138.2, 134.0, 132.1 (2 carbons), 129.3 (2 carbons), 128.7 (2 carbons), 128.6 (2 carbons), 128.5 (2 carbons), 128.3 (2 carbons),

128.0, 127.9 (6 carbons), 127.6, 99.6, 87.2, 80.0, 78.3, 75.5, 75.1, 73.3, 72.9, 72.7, 69.7, 69.3, 69.2 (2 carbons), 66.3, 62.7, 21.1, 20.9, 20.8, 20.6; ESI/APCI Calcd for $C_{47}H_{52}O_{14}SNa$ ($[M+Na]^+$) m/z 895.2975; measured m/z 895.2992.

Methyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-benzyl-4,6-benzylidene-α-D-mannopyranoside (73). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.6 (m, 30H), 5.63 (s, 1H, H-1'), 5.24 (s,1H, H-1"), 4.91 (d, *J* = 10.7 Hz, 1H), 4.79 (d, *J* = 11.9 Hz, 1H), 4.77 (s, 1H, H-1), 4.7 - 4.5 (m, 13H), 4.2 (m, 1H), 4.1 (m, 1H), 3.9 (m, 9H), 3.8 - 3.7 (m, 7H), 3.2 (m, 3H, OMe); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.6, 138.5, 138.4 (2 carbons), 137.7, 128.5, 128.4, 128.4, 128.3, 128.2, 127.8, 127.8, 127.6, 127.5, 126.2, 101.5, 101.0, 100.3, 79.6, 79.3, 77.3, 75.9, 75.3, 75.2, 75.0, 73.4, 73.3, 72.4, 72.1, 69.6, 69.0, 63.7, 54; ESI/APCI Calcd for $C_{55}H_{58}O_{11}Na$ ($[M+Na]^+$) m/z 917.3877; measured m/z 917.3853.

Methyl 2,3,4-tri O-benzyl-α-D-mannopyranoside (76).[111] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.3 – 7.4 (m, 15H), 4.96 (d, *J* = 10.9 Hz, 1H), 4.80 (d, *J* = 12.0 Hz, 1H), 4.67 – 4.73 (m, 5H), 3.98 (t, *J* = 9.4 Hz, 1H), 3.92 (dd, *J* = 2.9, 9.4 Hz, 1H, H-3), 3.85 (m, 1H), 3.81 (m, 2H), 3.65 (m, 1H, H-5), 3.32 (s, 3H, OCH_3), 2.01 (s, 1H, OH).

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (77). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 - 7.4 (m, 30H), 5.06 (d, *J* = 1.3 Hz, 1H), 4.95 (d, *J* = 10.7 Hz, 1H), 4.91 (d, *J* = 10.7 Hz, 1H), 4.7 (m, 4H), 4.6 - 4.7 (m, 5H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 1H), 3.8 – 4.0 (m, 7H), 3.8 (m, 1H), 3.8 - 3.6 (m, 4H), 3.25 (s, 3H, OMe), 1.92 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7 (2 carbons), 138.6, 138.5, 138.4, 138.3, 128.5 (4 carbons), 128.4 (5 carbons),

128.4 (2 carbons), 128.1 (2 carbons), 127.9 (2 carbons), 127.9 (2 carbons), 127.84, 127.80 (3 carbons), 127.7 (4 carbons), 127.6 (2 carbons), 99.0, 98.3, 80.3, 79.4, 75.2, 75.1, 75.0, 74.8, 74.7, 74.6, 72.9, 72.8, 72.3, 72.2, 71.7, 71.4, 66.2 (2 carbons), 62.4 (2 carbons), 54.8; ESI/APCI Calcd for $C_{55}H_{60}O_{11}Na$ ($[M+Na]^+$) m/z 919.4033; measured m/z 919.4054.

6′-Azidohexyl-2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (78). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.4 (m, 30H), 5.56 (dd, *J* = 1.0, 3.1 Hz, 1H, H-2'), 5.10 (d, *J* = 1.4 Hz, 1H), 4.86 (d, *J* = 10.3 Hz, 3H), 4.7 (m, 5H), 4.5 – 4.6 (m, 3H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.47 (d, *J* = 10.7 Hz, 1H), 4.42 (d, *J* =11.0 Hz, 1H), 4.0 (m, 3H), 3.7 -3.9 (m, 8H), 3.6 (m, 1H), 3.29 (m, 1H), 3.23 (t, *J* = 6.9 Hz, 2H), 2.13 (s, 3H, CH_3), 1.53 (m, 4H), 1.31 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 138.6, 138.55, 138.50, 138.46, 138.3, 138.1, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.62, 127.60, 99.7, 98.8, 79.8, 78.4, 75.3, 75.2, 75.0, 74.8, 74.5, 73.5, 73.4, 72.1, 72.0, 71.9, 69.4, 69.2, 68.8, 67.6, 51.5, 29.4, 28.8, 26.6, 25.8, 21.3; ESI/APCI Calcd for $C_{62}H_{71}N_3O_{12}Na$ ($[M+Na]^+$) m/z 1072.4935; measured m/z 1072.4923.

6′-azidohexyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (79). ^{1}H NMR ($CDCl_3$, 270 MHz) δ 7.1 – 7.4 (m, 30H), 5.17 (s, 1H, H-1′), 4.93 (s, 1H), 4.87 (d, *J* = 10.6 Hz, 1H), 4.84 (d, *J* = 10.9 hz, 1H), 4.5 – 4.8 (m, 10H), 4.15 (s, 1H), 3.7 – 4.05 (m, 10H), 3.6 (m, 1H), 3.5 (m, 1H), 3.3 (m, 1H), 3.2 (t, *J* = 6.9 Hz, 2H), 2.34 (s, 1H, OH), 1.55 (m, 4H), 1.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 68 MHz) δ 138.7, 138.6, 138.5, 138.4, 138.1, 128.6 (4 carbons), 128.5 (2 carbons), 128.4

(6 carbons), 128.1 (2 carbons), 127.9 (6 carbons), 127.8 (5 carbons), 127.7, 127.6, 127.55 (2 carbons), 127.5, 101.2, 98.9, 80.1, 79.9, 75.3, 75.1 (2 carbons), 74.9, 74.6, 73.5, 73.4, 72.3, 72.2, 72.0, 71.7, 69.5, 69.4, 68.6, 67.6, 51.5, 29.4, 28.8, 26.6, 25.8; ESI/APCI Calcd for $C_{60}H_{69}N_3O_{11}Na$ ($[M+Na]^+$) m/z 1030.4824; measured m/z 1030.4826.

6′-Azidohexyl -4,6-benzylidene-α-D-mannopyranoside (80). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.5 (m, 2H), 7.3 – 7.4 (m, 3H), 5.57 (s, 1H), 4.84 (d, *J* = 1.1 Hz, 1H, H-1), 4.27 (dd, *J* = 1.5, 4.0 Hz, 1H), 4.08 (dd, *J* = 3.4, 9.4 Hz, 1H), 4.02 (m, 1H), 3.9 (m, 1H, H-5), 3.8 (m, 2H) 3.7 (m, 1H), 3.4 (m, 1H), 3.28 (t, *J* = 6.9 Hz, 2H), 2.80 (s, 2H, 0H) 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 137.4, 129.5, 128.6 (2 carbons), 126.5 (2 carbons), 102.4, 100.4, 79.2, 71.2, 69.1, 68.9, 68.0, 63.3, 51.6, 29.5, 28.9, 26.7, 25.9; ESI/APCI Calcd for $C_{19}H_{27}N_3O_7Na$ ($[M+Na]^+$) m/z 416.1797; measured m/z 416.1785.

6'-Azidohexyl 3-*O*-pivaloyl-4,6-*O*-benzylidene-α-D-mannopyranoside (81). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.3 – 7.5 (m, 5H), 5.57 (s, 1H), 5.34 (dd, *J* = 3.4, 9.9 Hz, 1H, H-3), 4.84 (d, *J* = 1.4 Hz, 1H, H-1), 4.29 (dd, *J* = 3.4, 8.9 Hz, 1H, H-6), 4.0 – 4.1 (m, 2H), 3.8 – 3.9 (m, 2H), 3.7 (m, 1H), 3.4 (m, 1H), 3.28 (t, *J* = 6.9 Hz, 2H), 2.07 (d, 1H, OH), 1.6 (m 4H), 1.4 (m 4H), 1.23 (s, 9H, 3 CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.4, 137.3, 128.9, 128.5 (2 carbons), 125.9 (2 carbons), 100.45, 100.41, 76.4, 70.5, 70.2, 68.9, 67.9, 63.8, 51.5, 39.1, 29.3, 28.8, 27.2 (3 carbons), 26.6, 25.8; ESI/APCI Calcd for $C_{24}H_{35}N_3O_7Na$ ($[M+Na]^+$) m/z 478.2553; measured m/z 478.2566.

6'-Azidohexyl 2-*O*-pivaloyl-4,6-*O*-benzylidene-α-D-mannopyranoside (82). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.5 (m, 2H), 7.3 – 7.4 (m, 3H), 5.61 (s, 1H), 5.17 (dd, *J* = 1.4,

3.8 Hz, 1H, H-2), 4.73 (d, *J* = 1.3 Hz, 1H, H-1), 4.1 – 4.3 (m, 2H), 3.8 (m, 2H), 3.7 (m, 1H), 3.4 (m, 1H), 3.27 (t, *J* = 6.9 Hz, 2H), 2.18 (d, *J* = 4.5 Hz, 1H, OH), 1.6 (m, 4H), 1.4 (m, 4H), 1.27 (s, 9H, 3 CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.1, 137.2, 129.3, 128.4 (2 carbons), 126.3 (2 carbons), 102.3, 98.6, 79.6, 72.0, 68.9, 68.1, 67.6, 63.5, 51.4, 39.2, 29.3, 28.8, 27.3 (3 carbons), 26.6, 25.8; ESI/APCI Calcd for $C_{24}H_{35}N_3O_7Na$ ($[M+Na]^+$) m/z 500.2373; measured m/z 500.2380.

6'-Azidohexyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-pivaloyl-4,6-*O*-benzylidene-α-D-mannopyranoside (83). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.5 (m, 20H), 5.63 (s, 1H), 5.48 (dd, *J* = 1.7, 2.7 Hz, 1H), 5.25 (d, *J* = 1.7 Hz, 1H), 5.15 (dd, *J* = 1.4, 3.4 Hz, 1H), 4.84 (d, *J* = 11.4 Hz, 1H), 4.71 (d, *J* = 1.4 Hz, 1H), 4.70 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 11.0 Hz, 1H), 4.46 (d, *J* = 12.4 Hz, 1H), 4.42 (d, *J* = 11.4 Hz, 1H), 4.3 (m, 1H), 3.25 (t, *J* = 6.9 Hz, 2H), 2.09 (s, 3H, CH_3), 1.57 (m, 4H), 1.36 (m, 4H), 1.22 (s, 9H, $3CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 170.3, 138.8, 138.4, 138.0, 137.2, 128.9, 128.4 (2 carbons), 128.3 (2 carbons), 128.2 (3carbons), 127.9 (2 carbons), 127.8 (2 carbons), 127.7, 127.6 (2 carbons) 127.4, 126.0, 101.4, 99.2, 98.5, 79.3, 78.2, 77.3, 74.8, 74.1, 73.4, 71.9, 71.8, 71.7, 71.6, 68.9, 68.6, 68.5, 68.06, 63.6, 51.4, 39.0, 29.3, 28.8, 27.2 (3 carbons), 26.6, 25.7, 21.1; ESI/APCI Calcd for $C_{53}H_{65}N_3O_{13}Na$ ($[M+Na]^+$) m/z 974.4415; measured m/z 974.4433.

6'-Azidohexyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-4-*O*-benzyl-2-*O*-pivaloyl-α-D-mannopyranoside (84). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.4 (m, 20H), 5.36 (dd, *J* = 1.7, 3.1 Hz, 1H), 5.16 (d, *J* = 1.7 Hz, 1H), 5.06 (dd, *J* = 1.0, 3.1 Hz 1H), 4.86 (d, *J* = 11.7 Hz, 1H), 4.75 (d, *J* = 10.3 Hz, 1H), 4.69 (s, 1H), 4.62 (d, *J*

= 11.4 Hz, 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 12.4 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H) 4.43 (d, *J* = 12.4 Hz, 1H), 4.17 (dd, *J* = 3.1, 9.6 Hz, 1H), 3.96 (t, *J* = 9.6 Hz, 1H), 3.5-3.9 (m, 10H), 3.34 (m, 1H) 3.24 (t, *J* = 6.9 Hz, 2H), 2.12 (s, 3H, CH_3), 1.55 (m, 4H), 1.33 (m, 4H), 1.19 (s, 9H, $3CH_3$); ESI/APCI Calcd for $C_{53}H_{67}N_3O_{13}Na$ ($[M+Na]^+$) m/z 976.4572; measured m/z 976.4584.

Benzyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (85). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.4 (m, 5H), 5.38 (dd, *J* = 3.2, 10.0 Hz, 1H), 5.3 (m, 2H), 4.88 (s, 1H, H-1), 4.70 (d, *J* = 11.8 Hz, 1H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.26 (dd, *J* = 5.0, 12.2 Hz, 1H), 4.1 - 3.9 (m, 2H), 2.12 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.97 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.6, 170.0, 169.9, 169.8, 136.3, 128.9, 128.6, 128.3, 128.2, 96.8, 69.8, 69.6, 69.2, 68.7, 66.2, 62.4, 20.9, 20.8, 20.7 (2 carbons); ESI/APCI Calcd for $C_{21}H_{26}O_{10}Na$ ($[M+Na]^+$) m/z 461.1424; measured m/z 461.1429.

Benzyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (87).[114] ^1H NMR ($CDCl_3$, 400 MHz) δ 7.5 - 7.4 (m, 20H), 5.04 (d, *J* = 10.8 Hz, 1H) 5.01 (d, *J* = 1.6 Hz, 1H, H-1), 4.85 (d, *J* = 12.3 Hz, 1H), 4.8 - 4.7 (m, 5H), 4.51 (d, *J* = 11.9 Hz, 1H), 4.2 - 4.1 (m, 2H), 3.9 - 3.8 (m, 3H), 3.8 (m, 1H, H-5), 2.37 (t, *J* = 2.4 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.8, 138.7, 138.5, 137.5, 128.7, 128.7, 128.4, 128.2, 128.1, 128.0, 128.0, 127.9, 127.8, 97.8, 80.5, 75.6, 75.2, 75.1, 73.2, 72.8, 72.6, 69.4, 62.6.

Benzyl 6-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (88). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.2 - 7.4 (m, 35H), 5.13, (s, 1H, H-1), 4.97 (d, *J* = 10.6 H_Z, 1H), 4.94 (d, *J* = 11.0 Hz, 1H), 4.90 (d, *J* = 1.7 Hz, 1H, H-1'), 4.4 - 4.7 (m, 11H), 4.41 (d, *J* = 12.0 H_Z, 1H), 4.2 – 4.4 (m, 2H), 3.8 - 3.9

(m, 6H), 3.84 (m, 2H), 3.7 - 3.8 (m, 2H) 2.03 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.1, 138.7, 138.5 (3 carbons), 138.29, 138.24, 137.2, 128.56, 128.53 (8 carbons), 128.3, 128.2, 128.0 (4 carbons), 127.9 (4 carbons), 127.85, 127.80 (3 carbons), 127.7, 127.65 (2 carbons), 127.6, 98.1, 97.0, 80.4, 79.5, 75.2 (2 carbons), 74.9, 74.7 (2 carbons), 74.4, 72.9, 72.5, 72.3, 72.0, 71.6, 70.2, 68.9, 66.3, 63.6, 21.0; ESI/APCI Calcd for $C_{63}H_{66}O_{12}Na$ ($[M+Na]^+$) m/z 1037.4452; measured m/z 1037.4445.

Benzyl 2,3,4-tri-*O*-benzyl-6-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (89). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.2 - 7.4 (m, 35H), 5.10 (d, *J* = 1.4 Hz, 1H), 5.00 (d, *J* = 11.0 Hz, 1H), 4.92 (d, *J* = 1.7 Hz, 1H, H-1), 4.6 - 4.8 (m, 9H), 4.61 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 14.0 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 3.7 – 4.0 (m, 12H) 1.98 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.72, 138.70, 138.5 (2 carbons), 138.4, 138.2, 137.2, 128.6, 128.5 (10 carbons), 128.4 (2 carbons), 128.1, 128.0 (5 carbons), 127.9 (2 carbons), 127.8 (2 carbons), 127.7 (3 carbons), 127.6 (2 carbons), 98.4, 97.1, 80.4, 79.5, 75.3, 75.1, 74.90, 74.86, 74.7, 72.9, 72.8, 72.3 (2 carbons), 71.9, 71.7, 69.0, 66.3, 62.4; ESI/APCI Calcd for $C_{61}H_{64}O_{11}Na$ ($[M+Na]^+$) m/z 995.4346; measured m/z 995.4340.

Benzyl 6-*O*-(6-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (90). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 65H), 5.15 (s, 1H), 5.07 (s, 1H), 4.8 - 5.0 (m, 4H), 4.4 - 4.7 (m, 20H), 4.23 (m, 1H), 3.8 - 4.0 (m, 10H), 3.7 (m, 2H), 3.6 (m, 1H), 2.01 (s, 3H, CH_3), 1.99 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0 (2 carbons), 138.8 (2 carbons), 138.6 (2 carbons),, 138.5 (3 carbons),, 138.3, 138.2 (3 carbons), 137.2, 128.5

(2 carbons), 128.4 (8 carbons),, 128.31 (2 carbons), 128.30 (2 carbons), 128.1, 127.9 (8 carbons), 127.82 (2 carbons), 127.8 (2 carbons), 127.7 (3 carbons), 127.66 (3 carbons), 127.60, 102.4 (β), 98.3 (α), 98.1 (2 carbons, α/β), 97.0 (2 carbons, α/β), 81.9, 80.4, 79.6 (2 carbons), 79.3, 77.9, 77.3 (4 carbons), 75.2 (5 carbons), 74.8 (2 carbons), 74.7 (3 carbons), 74.5, 74.3 (2 carbons), 72.9, 72.8, 72.3, 72.2, 71.9, 71.8, 71.6, 71.3, 71.2, 70.1, 68.9 (2 carbons), 66.2, 65.9, 63.3, 20.9; ESI/APCI Calcd for $C_{90}H_{98}NO_{17}$ ($[M+NH_4]^+$) m/z 1464.6835; measured m/z 1464.6818.

Benzyl-2,3,4-tri-*O*-benzyl-6-*O*-(6-*O*-(2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (91). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 50H), 5.10 (d, *J* = 1.0 Hz, 1H), 5.08 (s, 1H), 4.94 (d, *J* = 11.0 Hz, 1H), 4.93 (d, *J* = 10.9 Hz, 1H), 4.90 (d, *J* = 1.6 Hz, 1H), 4.6 (m, 11H), 4.6 (m, 2H), 4.5 (m, 4H), 4.42 (d, *J* = 11.9 Hz, 1H), 3.9 (m, 10H), 3.8 (m, 2H), 3.6 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8 (2 carbons), 138.7, 138.6, 138.5 (2 carbons), 138.4, 138.3, 138.2, 137.2, 128.5 (2 carbons), 128.45 (6 carbons), 128.40 (4 carbons), 128.3 (4 carbons), 128.1 (2 carbons), 127.95 (4 carbons), 127.92 (4 carbons), 127.82 (2 carbons), 127.78 (2 carbons), 127.71 (4 carbons), 127.64 (4 carbons), 127.58 (2 carbons), 127.54 (2 carbons), 98.4, 98.3, 97.1, 80.4, 79.6, 79.4, 77.3 (2 carbons), 75.2 (5 carbons), 75.1 (3 carbons), 74.8 (2 carbons), 74.7 (2 carbons), 74. 67, 74.4, 72.9, 72.8, 72.7, 72.3 (4 carbons), 71.9, 71.7, 71.7, 71.6 (2 carbons), 71.5 (2 carbons); ESI/APCI Calcd for $C_{88}H_{92}O_{16}Na$ ($[M+Na]^+$) m/z 1427.6283; measured m/z 1427.6259.

6-*O*-(6-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-D-mannopyranose (92). ^{1}H NMR (D_2O, 400 MHz) δ 5.06 (s, 1H), 4.8 (m, 3H), 4.71 (s, 1H), 3.8 (m, 11H),

3.5 - 3.7 (m, 16H); ^{13}C NMR (D_2O, 75 MHz) δ 102.2 (β), 102.1, 101.9, 96.8, 96.4 (β), 84.3, 76.7 (β), 75.8 (β), 75.3 (2 carbons), 73.7 (β), 73.3 (3 carbons), 73.1 (4 carbons), 72.5 (2 carbons), 72.4 , 69.3 (2 carbons), 69.2 (2 carbons), 69.1 (2 carbons), 69.0 (β), 68.3 (β), 68.2 (2 carbons), 63.5; ESI/APCI Calcd for $C_{18}H_{32}O_{16}Na$ ($[M+Na]^+$) m/z 527.1588; measured m/z 527.1581

Methyl 6-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (93). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 30H), 5.10 (s, 1H), 4.92 (d, J = 10.9 Hz, 1H), 4.90 (d, J = 10.9 Hz, 1H), 4.4 – 4.7 (m, 11H), 4.2 (m, 2H), 3.86 -3.94 (m, 6H), 3.8 (m, 2H), 3.7 (m, 2H), 3.24 (s, 3H, OMe), 1.99 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.04, 138.6, 138.5 (2 carbons), 138.47, 138.3, 138.27, 128.5 (5 carbons), 128.4 (4 carbons), 128.3 (2 carbons), 128.1 (2 carbons), 127.9 (3 carbons), 127.8, 127.7 (4 carbons), 127.68 (2 carbons), 127.64 (2 carbons), 127.56, 99.02, 98.04, 80.4 (2 carbons), 79.3, 77.3, 75.1 (2 carbons), 74.8, 74.7, 74.6, 74.4, 72.9, 72.4, 72.2, 71.5 (4 carbons), 70.2, 66.2, 63.6, 54.8, 20.9; ESI/APCI Calcd for $C_{57}H_{62}O_{12}Na$ ($[M+Na]^+$) m/z 961.4139; measured m/z 961.4135.

Methyl 6-*O*-(6-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (94). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.10 (m, 45H), 5.51 (dd, *J* = 2.7, 4.8 Hz, 1H, H-2"), 5.10 (s, 1H, H-1"), 4.96 (s, 1H, H-1'), 4.95 (d, *J* = 10.9 Hz, 1H), 4.90 (d, *J* = 10.6 Hz, 1H), 4.83 (d, *J* = 10.9 Hz, 1H), 4.6 - 4.7 (m, 13H), 4.3 - 4.5 (m, 8H), 3.8 - 3.9 (m, 14H), 3.5 - 3.7 (m, 8H), 3.23 (s, 3H, OMe), 2.15 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 138.97, 138.91, 138.8, 138.7, 138.54, 138.50, 138.47, 138.1, 128.6 (6 carbons),

128.48 (5 carbons), 128.41 (4 carbons), 128.1 (2 carbons), 128.08 (2 carbons), 128.00 (3 carbons), 127.9 (4 carbons), 127.87 (4 carbons), 127.85 (4 carbons), 127.81 (4 carbons), 127.7 (2 carbons), 127.67 (4 carbons), 127.60, 127.5, 99.1, 98.3, 98.1, 80.5, 79.5, 77.9, 75.2 (2 carbons), 75.1, 75.02, 74.9, 74.7, 74.6, 74.3, 73.5, 73.04, 72.6, 72.3, 71.7, 71.6, 71.5 (2 carbons), 71.3, 68.9, 68.6, 66.7, 66.2, 21.4; ESI/APCI Calcd for $C_{84}H_{94}NO_{17}$ ($[M+NH_4]^+$) m/z 1388.6522; measured m/z 1388.6500.

Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(6-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (95). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 - 7.4 (m, 45H), 5.1 (m, 2H, H-1', H-1"), 4.9 (m, 3H), 4.8 (m, 2H), 4.4 - 4.7 (m, 27H), 4.1 (m, 1H), 3.8 - 3.9 (m, 17H), 3.6 - 3.7 (m, 11H), 3.3 (m, 3H, OMe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.93, 138.88, 138.78, 138.71, 138.6, 138.56, 138.51, 138.4, 138.1, 128.66 (3 carbons), 128.60 (5 carbons), 128.54 (4 carbons), 128.50 (5 carbons), 128.45 (3 carbons), 128.15 (2 carbons), 128.11 (5 carbons), 128.08 (5 carbons), 127.9 (2 carbons), 127.86 (3 carbons), 127.81 (5 carbons), 127.7 (2 carbons), 127.6, 99.9, 99.2, 98.1, 80.5, 79.8, 79.4, 77.4, 75.2 (3 carbons), 74.9, 74.7, 74.6, 74.4, 73.6, 73.1, 72.7, 72.3, 71.7 (2 carbons), 71.6 (2 carbons), 71.3, 69.0, 68.1, 66.3, 66.1, 54.9; ESI/APCI Calcd for $C_{82}H_{92}O_{16}N$ ($[M+NH_4]^+$) m/z 1346.6416; measured m/z 1346.6383.

Methyl-2,3,4-tri-*O*-benzyl-6-*O*-(6-*O*-(3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (epi-95). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (m, 2H), 7.2 - 7.4 (m, 41H), 7.1 (m, 2H), 5.31 (s, 1H), 5.07 (s, 1H), 4.99 (d, J = 12.2 Hz, 1H), 4.9 (d, J = 11.0 Hz, 1H), 4.89 (d, J = 11.4 Hz,

1H), 4.8 (m, 2H), 4.6 – 4.7 (m, 4H) 4.68 (m, 4H), 4.4 - 4.6 (m, 13H), 4.1 - 4.2 (m, 3H), 3.9 - 3.7 (m, 14H), 3.7 (m, 1H), 3.6 (m, 2H), 3.5 (m, 1H), 3.3 (m, 1H), 3.2 (m, 3H, OMe); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.9, 138.7, 138.6 (2 carbons), 138.5, 138.4, 138.2 (2 carbons), 138.0, 128.7 (2 carbons), 128.5 (2 carbons), 128.4 (8 carbons), 128.34 (2 carbons), 128.31 (2 carbons), 128.2 (2 carbons), 128.1 (2 carbons), 128.0 (2 carbons), 127.9 (2 carbons), 127.8 (4 carbons), 127.7 (4 carbons), 127.6 (4 carbons), 127.5, (2carbons), 102.2, 100.3, 98.9, 82.2, 80.4, 79.4, 77.9, 77.3 (2 carbons), 75.3, 75.1, 75.0 (3 carbons), 74.8, 74.4 (2 carbons), 74.3, 73.8, 73.4 (3 carbons), 72.7, 72.0, 71.4 2 (carbons) 71.3 (2 carbons), 69.0, 68.9, 67.8, 66.8, 54.7; ESI/APCI Calcd for $C_{82}H_{92}O_{16}N$ ($[M+NH_4]^+$) m/z 1346.6416; measured m/z 1346.6401.

Methyl-6-*O*-(6-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-manno-pyranoside (96). ^{1}H NMR (D_2O, 400 MHz) δ 4.80 (s, 1H), 4.78 (s, 1H), 4.70 (s, 2H), 4.64 (s, 1H), 3.8 (m, 7H), 3.7 (m, 6H), 3.6 (m, 10H), 3.29 (s, 3H, OMe), 3.23 (d, *J* = 2.2 Hz, 1H), 2.90 (s, 1H), 2.74 (s, 1H); ^{13}C NMR (D_2O, 100 MHz) δ 101.2, 99.6, 99.4, 72.9, 70.9 (2 carbons), 70.8, 70.7 (2 carbons), 70.1 (3 carbons), 66.9, 66.7, 66.6, 65.7, 65.6, 61.1, 54.9; ESI/APCI Calcd for $C_{19}H_{34}O_{16}Na$ ($[M+Na]^+$) m/z 541.1745; measured m/z 541.1736.

Methyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (97). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 - 7.5 (m, 30H), 5.53 (dd, *J* = 3.1, 1.8 Hz, 1H), 5.07 (d, *J* = 1.8 Hz, 1H), 4.84 (d, *J* = 10.9 Hz, 1H), 4.83 (d, *J* = 10.9 Hz, 1H), 4.76 (d, *J* = 2.0 Hz, 1H), 4.6 - 4.7 (m, 4H), 4.4 - 4.6 (m, 5H), 4.39 (d, *J* = 10.9 Hz, 1H), 3.7 - 4.0 (m, 11H), 3.24 (s, 3H), 2.10 (m, 3H); ^{13}C NMR ($CDCl_3$, 75

MHz) δ 170.2, 138.61, 138.58, 138.55, 138.46, 138.29, 138.09, 128.48 (3 carbons), 128.40 (5 carbons), 128.28 (2 carbons), 128.15 (2 carbons), 127.97 (3 carbons0, 127.8, 127.68 (3 carbons), 127.61 (3 carbons), 127.5 (3 carbons), 99.8, 99.6, 79.8, 78.2, 77.3, 75.2 (2 carbons), 74.7 (3 carbons), 74.4, 73.5 (2 carbons), 73.4 (2 carbons), 72.1 (2 carbons), 72.0 (2 carbons), 71.9 (2 carbons), 71.7 (2 carbons), 54.8, 21.2; HRFAB Calcd for $C_{57}H_{62}O_{12}Na$ ($[M+Na]^+$) m/z 961.4133; measured m/z 961.4148.

Methyl 3,4,6-tri-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (98). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4 (m, 30H), 5.16 (s, 1H, H-1'), 4.8 – 4.9 (m, 3H), 4.7 (m, 1H), 4.6 – 4.7 (m, 4H), 4.5 – 4.6 (m, 5H), 4.1 (m, 1H), 4.0 (m, 1H), 3.7 – 4.0 (m, 11H), 3.25 (s, 3H, O Me), 2.44 (d, *J* = 1.7 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 138.6, 138.5, 138.4, 138.3, 138.1, 128.6 (3 carbons), 128.4 (7 carbons), 127.99 (5 carbons), 127.96 (6 carbons), 127.8 (3 carbons), 127.7 (2 carbons), 127.6, 127.56 (2 carbons), 127.50, 101.2, 99.9, 80.1, 79.9, 75.2, 75.1, 74.9, 74.8, 74.5, 73.5, 73.4, 72.3, 72.2, 71.8, 71.7, 69.4, 69.3, 68.6, 54.8; ESI/APCI Calcd for $C_{55}H_{60}O_{11}Na$ ($[M+Na]^+$) m/z 919.4033; measured m/z 919.4030.

Methyl 2-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (99). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 -7.4 (m, 45H), 5.52 (d, *J* = 2.1 Hz, 1H), 5.18 (s, 1H), 5.04 (d, *J* = 1.7 Hz, 1H), 4.8 (m, 4H), 4.6 – 4.7 (m, 3H), 4.61 (m, 1H), 4.5 (m, 4H), 4.5 (m, 2H), 4.4 - 4.5 (m, 3H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.1 (m, 1H), 3.8 – 4.0 (m, 6H), 3.6 – 3.8 (m, 10H), 3.51 (d, *J* = 10.3 Hz, 1H), 3.22 (s, 3H, OMe), 2.12 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.1, 138.65 (2 carbons), 137.54 (3 carbons), 138.4 (2

carbons), 138.25, 138.1, 128.5 (8 carbons), 128.4 (3 carbons), 128.36 (3 carbons), 128.2 (3 carbons),128.10 (3 carbons), 127.97 (3 carbons), 127.96 (3 carbons), 127.90 (3 carbons), 127.88 (3 carbons), 127.7 (5 carbons), 127.68 (4 carbons), 127.5 (3 carbons), 100.8, 99.9, 99.8, 79.9, 78.3 (2 carbons), 77.4 (4 carbons), 75.3 (2 carbons), 75.2, 74.95, 74.94, 73.56 (3 carbons), 72.3, 72.29, 72.25, 72.1 (2 carbons), 71.8, 69.5 (2 carbons), 68.9 (2 carbons), 54.8, 21.4; ESI/APCI Calcd for $C_{84}H_{94}NO_{17}$ ($[M+NH_4]^+$) m/z 1388.6522; measured m/z 1388.6519.

Methyl-3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (100). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 45H), 5.25 (d, *J* = 1.6 Hz, 1H), 5.15 (d, *J* = 1.5 Hz, 1H), 4.8 (m, 4H), 4.70 (d, *J* = 12.1 Hz, 1H), 4.68 (d, *J* = 12.3 Hz, 1H), 4.6 (m, 4H), 4.5 (m, 6H), 4.49 (d, *J* = 10.7 Hz, 1H), 4.47 (d, *J* = 11.6 Hz, 1H), 4.36 (d, *J* = 12.2 Hz, 1H), 4.14 (s, 2H), 4.00 (t, *J* = 2.4 Hz, 1H), 3.9 (m, 5H), 3.8 (m, 2H), 3.8 (m, 4H), 3.7 (m, 2H), 3.6 (m, 1H), 3.6 (m, 1H), 3.25 (s, 3H, OMe), 2.46 (s, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.8 (2 carbons), 138.7 (3 carbons), 138.6, 138.5, 138.4, 138.3, 128.7 (4 carbons), 128.6 (2 carbons), 128.5 (8 carbons), 128.1 (8 carbons), 128.0 (5 carbons), 127.9 (2 carbons), 127.81 (2 carbons), 127.8 (2 carbons), 127.7 (5 carbons), 127.6 (2 carbons), 101.2, 101.0, 99.9, 80.2, 79.6 (2 carbons), 77.5, 75.3, 75.2 (3 carbons), 75.2 (3 carbons), 74.9, 74.5, 73.55 (2 carbons), 73.50 (3 carbons), 72.54, 72.5, 72.3, 71.9, 71.8, 71.7, 69.8, 69.6, 69.1, 68.7, 54.7; ESI/APCI Calcd for $C_{82}H_{92}NO_{16}$ ($[M+NH_4]^+$) m/z 1346.6391; measured m/z 1346.6397.

Methyl-2-*O*-(2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-α-D-manno-pyranoside (101). ^{1}H NMR (D_2O, 400 MHz) δ 5.15 (d, *J* = 1.0 Hz, 1H), 4.90 (d, *J* = 1.4 Hz, 1H), 4.85 (d, *J* = 1.0 Hz, 1H), 4.68 (s, 2H), 3.93 (s, 1H), 3.92 (s, 1H), 3.4 – 3.8 (m, 22H), 3.26 (s, 3H, OMe); ^{13}C NMR (D_2O, 100 MHz) δ 102.4, 100.8, 99.4, 78.9, 78.7, 73.4 (2 carbons), 72.7, 70.5, 70.3, 70.1 (2 carbons), 67.2, 67.1, 66.9, 61.3, 61.2, 61.1, 55.0; ESI/APCI Calcd for $C_{19}H_{34}O_{16}Na$ ($[M+Na]^+$) m/z 541.1745; measured m/z 541.1733.

Benzyl-2-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (102).[115] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.6 - 7.3 (m, 18H), 7.3 (m, 2H), 5.51 (s, 1H, H-2), 5.03 (s, 1H, H-1), 4.94 (d, *J* = 10.7 Hz, 1H), 4.78 (d, *J* = 11.4 Hz, 2H), 4.77 (d, *J* = 12.1 Hz, 1H), 4.6 - 4.5 (m, 4H), 4.11 (dd, *J* = 3.1, 8.8 Hz, 1H, H-2), 4.0 - 3.9 (m, 3H), 3.78 (broad, 1H), 2.21 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 138.7, 138.5, 138.3, 137.2, 128.7, 128.6, 128.6, 128.3, 128.2, 128.2, 128.0, 128.9, 127.9, 127.8, 97.4, 78.6, 75.5, 74.7, 73.7, 72.1, 71.9, 69.6, 69.2, 69.1.

Benzyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (103).[115] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.2 (m, 18H), 7.2 – 7.1 (m, 2H), 5.03 (d, *J* = 1.4 Hz, 1H, H-1), 4.86 (d, *J* = 10.8 Hz, 1H), 4.75 (d, *J* = 11.8 Hz, 1H), 4.71 (s, 2H), 4.69 (d, *J* = 11.2 Hz, 1H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.54 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 11.8 Hz, 1H), 4.11 (dd, *J* = 2.5, 4.4 Hz, 1H), 3.97 (m, 1H), 3.9 (m, 2H), 3.79 (dd, *J* = 3.9, 10.6 Hz, 1H), 3.74 (dd, *J* = 1.2, 10.9 Hz, 1H), 2.50 (d, *J* = 2.5 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.4, 138.0, 137.3, 128.6, 128.5, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 98.5, 80.4, 75.3, 74.4, 73.6, 72.1, 71.4, 69.2, 69.0, 68.5.

Benzyl 2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (104). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 - 7.4 (m, 35H) , 5.59 (d, *J* = 0.9 Hz, 1H, H-2), 5.11 (s, broad, 1H, H-1'), 5.00 (d, *J* = 0.9 Hz, 1H, H-1), 4.90 (d, *J* = 10.7 Hz, 1H), 4.88 (d, *J* = 10.8 Hz, 1H), 4.6 - 4.7 (m, 6H), 4.5 – 4.6 (m, 2H), 4.3 -4.5 (m, 4H), 4.08 (broad, 1H), 3.9 – 4.0 (m, 2H), 3.7 - 3.9 (m, 7H), 3.59 (d, *J* = 10.1 Hz, 1H), 2.16 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 138.75, 138.71, 138.6 (2 carbons), 138.4, 138.2, 137.5, 128.6 (4 carbons), 128.55 (5 carbons), 128.5 (4 carbons), 128.41 (2 carbons), 128.3 (2 carbons), 128.1 (2 carbons), 128.06 (2 carbons), 128.02 (3 carbons), 127.9 (2 carbons), 127.8, 127.76 (4 carbons), 127.71 (2 carbons), 127.6, 99.9, 98.2, 79.9, 78.4, 75.4, 75.3, 75.1, 74.9, 74.5, 73.6, 73.5, 72.3, 72.2, 72.0, 69.4, 69.2, 69.0, 68.9 (2 carbons), 21.4; ESI/APCI Calcd for $C_{63}H_{70}NO_{12}$ ($[M+NH_4]^+$) m/z 1032.4898; measured m/z 1032.4892.

Benzyl 3,4,6-tri-*O*-benzyl-2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (105). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 - 7.4 (m, 35H), 5.16 (s, 1H), 5.02 (s, 1H), 4.8 - 4.9 (m, 2H), 4.6 – 4.7 (m, 4H), 4.6 (m, 1H), 4.4 – 4.6 (m, 6H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.15 (s, 1H), 4.09 (s, 1H), 3.9 (m, 1H), 3.7 – 3.9 (m, 6H), 3.6 – 3.7 (m, 2H), 3.58 (d, *J* = 10.7 Hz, 1H), 2.42 (d, *J* = 2.1 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7, 138.5 (2 carbons), 138.3 (2 carbons), 138.1, 137.4, 128.7, 128.6 (3 carbons), 128.5 (5 carbons), 128.4 (5 carbons), 128.1, 128.09 (3 carbons), 127.9, 127.86 (3 carbons), 127.82 (3 carbons), 127.7 (4 carbons), 127.6 (2 carbons), 127.5, 101, 98.3, 80.1, 79.8, 75.3, 75.07, 75.0, 74.9, 74.4 (2 carbons), 73.5, 73.4, 72.4, 72.3, 72.2, 71.6,

69.4, 69.1 (2 carbons), 69.0, 68.6 (2 carbons); ESI/APCI Calcd for $C_{61}H_{64}O_{11}N$ ($[M+NH_4]^+$) m/z 995.4346; measured m/z 995.4354.

Benzyl 2-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (106). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 - 7.4 (m, 50H), 5.55 (dd, *J* = 1.8, 3.2 Hz, 1H, H-2"), 5.19 (d, *J* = 1.6 Hz, 1H, H-1"), 5.06 (d, *J* = 1.6 Hz, H-1'), 5.02 (d, *J* = 1.7 Hz, 1H, H-1), 4.8 - 4.9 (m, 3H), 4.71 (d, *J* = 11.6 Hz, 2H), 4.5 - 4.7 (m, 9H), 4.5 (m, 1H), 4.41 (d, *J* = 10.9 Hz, 1H), 4.33 (d, *J* =11.7 Hz, 1H), 4.30 (d, *J* =12.0 Hz, 1H), 4.1 (m, 1H), 4.03 (m, 2H), 3.8 - 3.9 (m, 6H), 3.7 - 3.8 (m, 5H), 3.6 - 3.7 (m, 5H), 3.52 (d, *J* = 10.5 Hz, 1H), 2.14 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 138.8 (2 carbons), 138.7 (2 carbons), 138.6 (2 carbons), 138.5, 138.4, 138.2, 137.6, 128.6 (3 carbons), 128.5 (6 carbons), 128.4 (3 carbons), 128.4 (2 carbons), 128.2 (4 carbons), 128.0 (4 carbons), 127.9 (4 carbons), 127.8 (3 carbons), 127.7 (5 carbons), 127.7 (6 carbons), 100.9, 99.6, 98.4, 79.7 (2 carbons), 79.5, 78.4 (2 carbons), 77.5 (3 carbons), 75.3 (4 carbons), 75.2 (2 carbons), 75.1, 74.9, 74.4, 73.5, (5 carbons) 72.3, (2 carbons), 72.2, 72.1, (3 carbons), 69.5 (2 carbons), 69.3, 68.9 (3 carbons), 21.9; ESI/APCI Calcd for $C_{90}H_{98}NO_{17}$ ($[M+NH_4]^+$) m/z 1464.6835; measured m/z 1464.6838.

Benzyl-3,4,6-tri-*O*-benzyl-2-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (107). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 - 7.4 (m, 50H), 5.21 (d, *J* = 1.7 Hz, 1H, H-1"), 5.13 (d, *J* = 1.4 Hz, 1H, H-1'), 5.03 (d, *J* = 1.7 Hz, 1H, H-1), 4.82 (d, *J* =11.0 Hz, 1H), 4.80 (d, *J* = 10.7 Hz, 1H), 4.7 - 4.4 (m, 16H), 4.34 (d, *J* = 11.7 Hz, 1H), 4.31 (d, *J* = 12.0 Hz, 1H),

4.12 (s, 2H), 4.02 (s, 1H), 3.8 - 3.9 (m, 7H), 3.5 - 3.8 (m, 8H), 2.36 (d, *J* = 2.4 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.7 (2 carbons), 138.6 (2 carbons), 138.5, 138.4 (2 carbons), 138.3, 138.1, 137.5, 128.55 (3 carbons), 128.5 (2 carbons), 128.4 (9 carbons), 128.1 (2 carbons), 127.9 (8 carbons), 127.86 (3 carbons), 127.79 (4 carbons), 127.72 (5 carbons), 127.6 (5 carbons), 127.5 (2 carbons), 101.1, 101.0, 98.3, 80.1, 79.5, 77.3 (2 carbons), 75.4, 75.2 (2 carbons), 75.1, 75.0, 74.9 (2 carbons), 74.4, 73.4 (2 carbons), 73.3 (3 carbons), 72.4 (2 carbons), 72.3, 72.2 (2 carbons), 72.1, 71.96, 71.67, 69.5, 69.4, 69.16 (2 carbons), 69.03, 68.63 (2 carbons); ESI/APCI Calcd for $C_{88}H_{96}NO_{16}$ ($[M+NH_4]^+$) m/z 1422.6729; measured m/z 1422.6729.

2-*O*-(2-*O*-(α-D-mannopyranosyl)-α-D-mannopyranosyl)-D-mannopyranose (108). ^{1}H NMR (D_2O, 400 MHz) δ 5.26 (s, 1H), 5.19 (s, 1H), 4.93 (s, 2H), 3.5 – 4.0 (m, 28H); ^{13}C NMR (D_2O, 100 MHz) δ 102.4, 100.7, 92.6, 79.5, 78.7, 73.4 (2 carbons), 72.6, 70.5, 70.1 (3 carbons), 67.2 (2 carbons), 66.9, 61.2 (2 carbons), 61.1; ESI/APCI Calcd for ESI/APCI Calcd for $C_{18}H_{32}O_{16}Na$ ($[M+Na]^+$) m/z 527.1588; measured m/z 527.1577.

Methyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (109). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.5 (m, 25H), 5.64 (s, 2H, H-1', H-2), 5.33 (s, 1H, H-1), 4.90 (d, *J* = 10.8 Hz, 2H), 4.74 (d, *J* = 12.2 Hz), 4.72 (s, 1H, H-1), 4.6 - 4.7 (m, 5H), 4.4 - 4.5 (m, 4H), 4.2 - 4.3 (m, 4H), 4.00 (dd, *J* = 3.2, 12.1 Hz, 2H), 3.6 - 3.9 (m, 9H), 3.31 (s, 3H, OMe). 2.11 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 138.8, 138.6, 138.1, 138.0, 137.6, 128.9, 128.7, 128.5, 128.4 (3 carbons), 128.30 (2 carbons), 128.28 (2 carbons), 128.0 (4 carbons), 127.9 (4 carbons), 127.7 (2 carbons), 126.2 (2 carbons), 101.4, 100.5, 99.0, 79.3, 78.1,

77.4 (4 carbons), 75.2, 74.5, 73.8, 73.6, 73.4, 72.4, 71.7, 68.9, 68.4, 64.1, 60.6, 55.0, 21.2; ESI/APCI Calcd for $C_{50}H_{54}O_{12}Na$ ($[M+Na]^+$) m/z 869.3513; measured m/z 869.3507.

Methyl-3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (110). The starting material, methyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (0.72 g, 0.85 mmol) and cupper triflate (0.03 g, 0.085 mmol) were dissolved in 10 mL dichloromethane and borane tetrahydrofuran complex (1.0 mL) was added and the mixture was stirred for 2 hr at room temperature. When complete, reaction was quenched with methanol, filtered off precipitate, concentrated and purified resulting residue. Product (0.71 g) was obtained in 98 % yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 25H), 5.52 (d, *J* = 1.7 Hz, 1H, H-2), 5.23 (s, 1H, H-1), 4.90 (d, *J* = 11.2 Hz, 1H), 4.81 (d, *J* = 10.9 Hz, 1H), 4.6 - 4.7 (m, 8H), 4.4 - 4.5 (m, 4H), 4.1 - 4.2 (m, 3H), 3.6 – 4.0 (m); 3.28 (s, 3H, OMe), 2.11 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 138.8, 138.5, 138.3, 138.1, 138.0, 128.7 (5 carbons), 128.6 (2 carbons), 128.4 (5 carbons), 128.3 (2 carbons), 128.2 (3 carbons), 128.0, 127.9 (2 carbons), 127.88 (4 carbons), 127.74 (2 carbons), 127.71, 99.8, 98.9, 78.26, 78.1, 77.4, 75.4, 75.2, 75.14, 74.6, 73.7, 72.7, 72.4, 72.3, 71.9, 69.4, 68.9, 62.3, 55.04, 21.2; ESI/APCI Calcd for $C_{50}H_{56}O_{12}Na$ ($[M+Na]^+$) m/z 871.3664; measured m/z 871.3650.

Methyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(3,6-di-*O*-acetyl-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (111). The acceptor, methyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-

mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (0.70 g, 0.836 mmol) and donor, phenyl 3,4-di-*O*-acetyl-2,4-*O*-dibenzyl-1-thio-α-D-mannopyranoside (0.50 g, 0.92 mmol) were dissolved in 8 mL dichloromethane. NIS (0.226 g, 1.00 mmol) and TMSOTf (22.71 μL, 0.125 mmol) were added and the mixture was sonicated for 10 min. TLC showed reaction is complete. The reaction mixture was quenched by adding sodium thiosulfate and sodium bicarbonate solid and letting it stir for some hours or until solution turn yellow. The solid residue was filtered off and washed with excess ethyl acetate, then the filtrate was concentrated, and purified in a chromatography column. The product (1.05 g) was obtained in 98% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.1 - 7.3 (m, 35H), 5.51 (s, 1H, H-2"), 5.31 (s, 1H, H-1"), 5.21 (s, 1H, H-3'"), 5.11 (d, *J* = 1.8 Hz, 1H, H-1"), 4.88 (d, *J* = 10.9 Hz, 1H), 4.83 (d, *J* = 11.1 Hz, 1H), 4.5 - 4.7 (m, 9H), 4.4 - 4.5 (m, 3H), 4.39 (d, *J* = 12.2 Hz, 1H), 4.1 (m, 1H), 3.6 – 4.0 (m, 15H), 3.25 (s, 3H, OMe), 2.08 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.98 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.9, 170.1 (2 carbons), 138.7, 138.4, 138.3, 138.2, 138.1, 138.07, 137.9, 128.5 (7 carbons), 128.4 (2 carbons), 128.3 (6 carbons), 127.9 (4 carbons), 127.8 (3 carbons), 127.7 (2 carbons), 127.65 (3 carbons), 127.6 (3 carbons), 99.8, 98.6, 97.7, 78.1 (2 carbons), 77.9, 77.3 (6 carbons), 76.3, 75.2 (2 carbons), 74.9, 74.8, 74.4, 73.8, 73.5, 73.3, 72.7, 72.6, 72.3, 71.9 (2 carbons), 69.8, 69.2, 68.8, 63.4, 54.8, 21.2, 21.1, 20.9; ESI/APCI Calcd for $C_{74}H_{82}O_{19}Na$ ($[M+Na]^+$) m/z 1297.5348; measured m/z 1297.5328.

Methyl-6-*O*-(2,4-di-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (112). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 35H), 5,26 (s, 1H), 5.15 (s, 1H), 4.94 (d, *J* = 11.1 Hz,

1H), 4.86 (d, *J* = 11.1 Hz, 1H), 4.77 (d, *J* = 11.0 Hz, 1H), 4.5 - 4.7 (m, 11H), 4.42 (d, *J* = 11.8 Hz, 1H), 4.1 (m, 1H), 3.6 – 4.0 (m, 18H), 3.27 (s, 3H, OMe), 2.39 (s, 1H, OH), 2.33 (d, *J* = 9.4 Hz, 1H, OH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.7, 138.6, 138.5, 138.4, 138.2, 138.0 (2 carbons), 128.7 (5 carbons), 128. 6 (4 carbons), 128.4 (4 carbons), 128.1 (2 carbons), 128.0 (2 carbons), 127.97 (3 carbons), 127.9 (4 carbons), 127.79 (4 carbons), 127.76 (3 carbons), 127.6 (2 carbons), 127.56, 101.5, 98.7, 97.5, 80.2, 78.9, 77.7, 76.7, 75.2 (4 carbons), 75.0, 74.6, 73.7 (2 carbons), 72.9, 72.7, 72.3, 72.2, 71.9 (2 carbons), 71.6, 69.5, 68.9, 66.2, 62.4, 55.0; ESI/APCI Calcd for $C_{68}H_{76}O_{16}Na$ ($[M+Na]^+$) m/z 1171.5031; measured m/z 1171.5005.

Methyl 3-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(3,6-di-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (113). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.4 – 7.1 (m, 80H), 5.51 (s, broad, 3H), 5.21 (s, 2H), 5.01 (s, 1H), 4.98 (s, 1H), 4.96 (s, 1H), 4.7 – 4.9 (m, 5H), 4.72 (d, *J* = 11.3 Hz, 2H), 4.3 – 4.7 (m, 28H), 4.30 (d, *J* = 12.0 Hz, 2H), 4.25 (d, *J* = 12.0 Hz, 1H), 4.0 – 4.2 (m, 3H), 3.4 – 4.0 (m, 28H), 3.35 (d, *J* = 10.3 Hz, 1H), 3.17 (s, 3H, OMe), 2.14 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.06 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 170.2 (2 carbons), 138.8 (2 carbons), 138.7, 138.6 (2 carbons), 138.5 (2 carbons), 138.3 (4 carbons), 138.18 (2 carbons), 138.16, 137.96, 137.89, 128.6 (2 carbons), 128.47 (8 carbons), 128.40 (8 carbons), 128.3 (6 carbons), 128.29 (10 carbons), 128.16 (3 carbons), 127.89 (8 carbons), 127.86 (6 carbons), 127.78 (3 carbons), 127.67 (4 carbons), 127.56 (4 carbons), 127.55 (5 carbons), 127.48 (4 carbons), 127.29 (2 carbons), 101.2,

99.8, 99.5, 98.4, 98.1, 97.0, 79.8, 78.3 (2 carbons), 78.2 (2 carbons), 77.8 (2 carbons), 77.3 (3 carbons), 75.09 (2 carbons), 74.98 (3 carbons), 74.8 (2 carbons), 74.76, 74.74, 74.16 (4 carbons), 73.46 (2 carbons), 73.44 (3 carbons), 73.25 (2 carbons), 72.8, 72.25 (4 carbons), 72.12 (3 carbons), 71.92 (2 carbons), 72.90 (2 carbons), 71.63 (2carbons), 71.5, 71.3 (2 carbons), 71.0, 68.8 (3 carbons), 68.4 (2 carbons), 54.8, 21.26 (2 carbons), 21.2; ESI/APCI Calcd for $C_{155}H_{170}O_{34}N$ ($[M+NH_4]^+$) m/z 2589.1599; measured m/z 2589.1604.

Methyl-3-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (114). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.4 (m, 80H), 5.25 (s, 2H), 5.20 (s, 1H), 5.09 (s, 1H), 5.05 (s, 1H), 4.82 (s, 1H), 4.8 (m, 6H), 4.4 – 4.7 (m, 35H), 4.34 (d, *J* = 11.7 Hz, 1H), 4.31 (d, *J* = 12.4 Hz, 1H), 4.1 (m, 4H), 4.05 (m, 2H), 3.4 – 4.0 (m, 40H), 3.18 (s, 3H, OCH_3), 2.34 (s, broad, 3H, OH); ESI/APCI Calccd for $C_{149}H_{160}O_{31}Na$ ($[M+Na]^+$) m/z 2468.0836; measured m/z 2468.0746.

6'-Azidohexyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (115).[78] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.37 (dd, *J* = 3.4, 9.9 Hz, 1H, H-3), 5.28 (t, *J* = 9.9 Hz, 1H, H-4), 5.24 (dd, *J* = 1.4, 3.4 Hz, 1H, H-2), 4.80 (d, *J* = 1.4 Hz, 1H, H-1), 4.29 (dd, *J* = 5.4, 12.2 Hz, 1H, H-6), 4.10 (dd, *J* = 2.3, 12.2 Hz, 1H, H-6′), 3.98 (m, 1H, H-5), 3.68 (m, 1H), 3.45 (m, 1H), 3.28 (t, J = 6.9 Hz, 2H), 2.16 (s, 3H), 2.11 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H), 1.62 (m, 4H), 1.40 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 170.3, 170.1, 169.9,

97.8, 69.9, 69.3, 68.7, 68.5, 66.5, 62.7, 51.5, 29.3, 28.9, 25.9, 25.5, 21.1, 20.9, 20.8 (3 carbons).

6'-Azidohexyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (117). The starting material, 6′-azidohexyl-4,6-O-benzylidene-α-D-mannopyranoside (1.35 g, 3.43 mmol) was dissolved in 15 mL dichloromethane and tetrabutylammonium hydrogen sulfate (0.35 g, 1.03 mmol) was added followed by benzyl bromide (0.45 ml, 3.77 mmol) and 1N NaOH (6 mL). The mixture was refluxed for 15 hr, and then it was diluted with dichloromethane, and washed with water, and brine. The mixture was then dried over Na_2SO_4, filtered, concentrated and purification gave product (0.71 g) in 58% yield. A byproduct **118** was also obtained and some starting material was left. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.5 - 7.6 (m, 2H), 7.3 - 7.4 (m, 8H), 5.59 (s, 1H, H-1'), 4.84 (d, *J* = 1.2 Hz, H-1, 1H,), 4.76 (d, *J* = 11.8 Hz, 1H), 4.72 (d, *J* = 11.8 Hz, 1H), 4.26 (dd, *J* = 3.7, 9.1 Hz, H-6, 1H), 4.10 (m, 1H, H-5), 3.93 (t, *J* = 9.0 Hz, H-4, 1H), 3.8 - 3.7 (m, 3H), 3.6 (m, 1H), 3.3 (m, 1H), 3.28 (t, *J* = 6.9 Hz. 2H), 2.38 (d, 1H, OH), 1.61 (m, 4H), 1.39 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 137.5, 129.3, 128.8 (2 carbons), 128.5 (2 carbons), 128.3, 128.2 (2 carbons), 126.4 (2 carbons), 102.3, 98.5, 79.8, 78.9, 73.9, 69.0, 68.9, 67.9, 63.7, 51.6, 29.4, 28.9, 26.7, 25.9; ESI/APCI Calcd for $C_{26}H_{33}N_3O_6Na$ ($[M+Na]^+$) m/z 506.2267; measured m/z 506.2281.

6'-Azidohexyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (118). Please refer to compound **117**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (m, 2H), 7.4 - 7.3 (m, 8H) 5.64 (s, 1H, H-1'), 4.90 (d, *J* = 11.9 Hz, 1H), 4.88 (s, 1H, H-1), 4.74 (d, *J* = 11.8 Hz, 1H), 4.28 (m, 1H), 4.11 (t, *J* = 9.2 Hz, 1H, H-4), 4.07 (dd, *J* = 1.7, 3.2 Hz, 1H, H-2), 3.94

(dd, *J* = 3.4, 9.6 Hz, 1H, H-3), 3.8 (m, 2H), 3.7 (m, 1H), 3.4 (m, 1H), 3.28 (t, *J* = 6.9 Hz, 2H), 2.67 (s, 1H, OH), 1.6 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.3, 137.7, 129.1, 128.7, 128.4, 128.1, 127.9, 126.4, 126.2, 101.7, 100.1, 76.1, 75.9, 73.3, 70.3, 69.1, 67.9, 63.5, 51.6, 29.5, 28.9, 26.7, 25.9; ESI/APCI Calcd for $C_{26}H_{33}N_3O_6Na$ ($[M+Na]^+$) m/z 506.2267; measured m/z 506.2273.

6'-Azidohexyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (119). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.4 - 7.6 (m, 3H,), 7.1 - 7.3 (m, 22H), 5.65 (s, 1H), 5.63 (d, *J* = 1.9 Hz, 1H), 5.34 (s, 1H), 4.90 (d, *J* = 10.9 Hz, 2H), 4.77 (s, 2H), 4.73 (d, *J* = 5.4 Hz, 1H), 4.6 (m, 3H), 4.4 - 4.5 (m, 4H), 4.2 (m, 2H), 4.0 (m, 1H), 3.7 - 3.9 (m, 3H), 3,5 - 3.6 (m, 2H), 3.3 (m, 1H), 3.24 (t, *J* = 6.9 Hz, 2H), 2.11 (s, 3H, CH_3), 1.5 (m, 4H), 1.4 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 138.8, 138.5, 138.1 (2 carbons), 137.6, 128.9, 128.7 (2 carbons), 128.6 (3 carbons), 128.5 (4 carbons), 128.4 (3 carbons), 128.3 (2 carbons), 128.3 (3 carbons), 128.0 (4 carbons), 127.9 (3 carbons), 127.7 (2 carbons), 126.2 (2 carbons), 101.4, 99.4, 99.1, 79.3, 78.1, 77.8 (2 carbons), 77.4 (2 carbons), 75.2, 74.4, 73.8, 73.7, 73.5 (2 carbons), 72.4, 71.7, 69.1, 68.9, 68.4, 67.8, 64.3, 51.6, 29.4, 28.9, 26.7, 25.9, 21.2; ESI/APCI Calcd for $C_{55}H_{67}N_4O_{12}$ ($[M+NH_4]^+$) m/z 975.4755; measured m/z 975.4774

6'-Azidohexyl 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl -α-D-mannopyranoside (120). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 - 7.4 (m, 25H), 5.50 (s, 1H, H-2'), 5.22 (s, 1H, H-1'), 4.90 (d, *J* = 10.9 Hz, 1H), 4.81 (d, *J* = 10.9 Hz, 1H), 4.75 (s, 1H, H-1), 4.6 – 4.7 (m, 5H), 4.4 - 4.5 (m, 3H), 4.15 (dd, *J* = 2.8, 9.4 Hz,

1H), 3.9 – 4.0 (m, 3H), 3.6 – 3.9 (m, 10H), 3.3 (m, 1H), 3.24 (t, *J* = 6.9 Hz, 2H), 2.11 (s, 3H, CH_3), 1.53 (m, 4H), 1.32 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 138.8, 138.4, 138.3, 138.1, 137.9, 128.7 (2 carbons), 128.6 (2 carbons), 128.6 (2 carbons), 128.4 (4 carbons), 128.3 (2 carbons), 128.29 (2 carbons), 128.1, 127.98 (2 carbons), 127.90 (2 carbons), 127.8 (2 carbons), 127.74, 127.71 (2 carbons), 99.9, 97.7, 78.9, 78.1, 77.9, 77.4, 75.5, 75.2, 75.1, 74.6, 73.6, 72.6, 72.4 (2 carbons), 72.0, 69.3, 69.0, 67.8, 62.3, 51.6, 29.5, 28.9, 26.7, 25.9, 21.1; ESI/APCI Calcd for $C_{55}H_{65}N_3O_{12}Na$ ($[M+Na]^+$) m/z 982.4466; measured m/z 982.4453.

6′-Azidohexyl- 3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-benzyl-α-D-mannopyranoside (121). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.4 (m, 20H), 5.42 (s, broad, 2H, H -1', H-2'), 4.87 (d, *J* = 11.4 Hz, 1H), 4.76 (d, *J* = 1.4 Hz, 1H, H – 1), 4.70 (d, *J* = 11.0 Hz, 1H), 4.5 – 4.6 (m, 4H), 4.48 (d, *J* = 12.0Hz, 1H), 4.46 (d, *J* = 11.0Hz, 1H), 3.9 -4.1 (m, 4H), 3.5 -3.9 (m, 10H), 3.3 (m, 1H), 3.25 (t, *J* = 6.9 Hz, 2H), 3.16 (s, 1H, OH) 2.09 (s, 3H, CH_3), 1.54 (m, 4H), 1.33 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.5, 138.5, 137.9 (2 carbons), 137.9, 128.5 (2 carbons), 128.4, 128.37, 128.2, 127.9, 127.8 (2 carbons), 127.71, 127.70, 98.3, 97.5, 78.8, 78.4, 77.9, 74.9, 74.6, 73.6, 72.6, 72.3, 71.9, 71.7, 69.5, 69.1, 67.6, 67.0, 62.9, 51.5, 29.3, 28.8, 26.6, 25.8, 21.1; ESI/APCI Calcd for $C_{48}H_{59}N_3O_{12}Na$ ($[M+Na]^+$) m/z 892.3996; measured m/z 892.4001.

6′-Azidohexyl-6-*O*-(6-*O*-acetyl-3-*O*-benzoyl-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (122). ^1H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H), 7.6 (m, 1H), 7.5 – 7.1 (m, 37H), 5.59 (dd, *J* = 2.7, 9.2 Hz, 1H, H-3), 5.52 (s, 1H, H-2), 5.24 (s, 1H, H-1),

5.16 (s, 1H, H-1), 4.87 (d, *J* = 11.0 Hz, 2H), 4.8 – 4.3 (m, 15H), 4.1 – 3.6 (m, 15H), 3.3 (m, 1H), 3.21 (t, *J* = 6.9 Hz, 2H), 2.1 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 1.5 (m, 4H), 1.3 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 170.3, 165.6, 138.9, 138.5, 138.4, 138.2, 137.9, 133.3, 132.7, 130.3, 129.9, 128.7, 128.4, 128.4, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 99.9, 98.0, 97.4, 78.9, 78.2, 77.9, 76.6, 75.7, 75.4, 75.3, 75.1, 74.6, 73.6, 73.5, 73.3, 72.9, 72.6, 72.4, 72.2, 72.1, 70.0, 69.3, 69.1, 67.7, 66.0, 63.5, 51.6, 29.5, 28.9, 26.7, 25.9, 21.2, 21.1; ESI/APCI Calcd for $C_{84}H_{97}N_4O_{19}$ ($[M+Na]^+$) m/z 1465.6747; measured m/z 1465.6711.

6′-Azidohexyl-6-*O*-(2,4-di-*O*-benzyl-α-D-mannopyranosyl)-3-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (123). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.6 – 7.4 (m, 35H), 5.49 (s, 1H), 5.38 (s, 1H), 5.16 (d, *J* = 11.1 Hz, 1H), 5.07 (d, *J* = 11.1 Hz, 1H), 4.9 (m, 2H), 4.8 (m, 8H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.71 (d, *J* = 12.2 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.39 (dd, *J* = 2.8, 9.5 Hz, 1H), 4.3 (m, 2H), 4.1 (m, 8H), 3.9 (m, 7H), 3.8 (m, 1H), 3.5 (m, 1H), 3.45 (t, *J* = 6.9 Hz, 2H), 2.60 (s 1H, OH), 2.54 (d, *J* = 9.4 Hz, 1H, OH), 2.18 (s, 1H, OH), 1.7 (m, 4H), 1.5 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.6, 138.5, 138.4, 138.3, 138.1, 137.9 (2 carbons), 128.75 (2 carbons), 128.71 (4 carbons), 128.6 (4 carbons), 128.4 (2 carbons), 128.2 (2 carbons), 128.1 (2 carbons), 128.0 (2 carbons), 127.9 (2 carbons), 127.88 (4 carbons), 127.82, 127.7 (3 carbons), 101.5, 97.5, 97.4, 80.1, 78.9, 77.8, 77.4, 76.7, 75.3, 75.2 (2 carbons), 75.0, 74.5, 73.5 72.8, 72.6, 72.3 (2 carbons), 72.2, 72.1, 72.0, 71.6, 71.5, 69.3, 68.9, 67.7, 66.1, 62.3, 51.4, 29.3, 28.8, 26.6, 25.8; ESI/APCI Calcd for $C_{73}H_{85}N_3O_{16}Na$ ($[M+Na]^+$) m/z 1282.5828; measured m/z 1282.5790.

6′-Azidohexyl 3-*O*-(2-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(3,6-di-*O*-(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (124). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.1 – 7.4 (m, 80H), 5.53 (m, 3H), 5.27 (s, 2H), 5.09 (d, *J* = 1.7 Hz, 1H), 5.04 (s, 1H), 5.00 (d, *J* = 1.7 Hz, 1H), 4.8 – 4.92 (m, 6H), 4.78 (d, *J* = 9.6 Hz, 1H), 4.5 – 4.73 (m, 18H), 4.4 – 4.5 (m, 10H), 4.2 – 4.33 (m, 2H), 3.7 – 4.2 (m, 25H), 3.5 – 3.7 (m, 15H), 3.33 (d, *J* = 9.9 Hz, 1H), 3.24 (m, 1H), 3.16 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 1.4 (m, 4H), 1.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.3, 170.2 (2 carbons), 138.8, 138.77, 138.71, 138.6, 138.57, 138.52, 138.45 (2 carbons), 138.40, 138.3 (3 carbons), 138.2 (2 carbons), 138.1, 137.9, 137.89, 128.7, 128.5 (4 carbons), 128.4 (8 carbons), 128.3 (10 carbons), 128.2, 127.9 (6 carbons), 127.7 (2 carbons), 127.6 (2 carbons), 127.56 (2 carbons), 127.51, 127.45 92 carbons), 127.40, 127.2, 101.3, 99.8, 99.4, 98.4, 97.0 (2 carbons), 80.1, 80.0, 78.3, 78.2 (2 carbons), 77.8, 77.4, 75.2, 75.1, 74.9 (2 carbons), 74.7 (2 carbons), 74.1 (3 carbons), 73.4 (4 carbons), 73.2, 72.2 (2 carbons), 72.17, 72.1 (2 carbons), 71.98, 71.92, 71.7, 71.3, 71.0, 69.7, 68.9 (3 carbons), 68.7 (4 carbons), 68.4 (2 carbons), 68.3, 67.6, 66.2, 65.9, 51.4, 29.3, 28.8, 26.6, 25.8, 21.3 (2 carbons), 21.1; ESI/APCI Calcd for $C_{160}H_{175}N_3O_{34}Na$ ($[M+Na]^+$) m/z 2705.1949; measured m/z 2705.1872.

6′-Azidohexyl 3-*O*-(2-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-6-*O*-(3,6-di-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-mannopyranosyl)-2,4-di-*O*-benzyl-α-D-

mannopyranoside (125). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 80H), 5.30 (s, 1H), 5.22 (s, 1H), 5.16 9 (s, 2H), 4.99 9s, 1H), 4.8 – 4.9 (m, 6H), 4.4 – 4.8 (m, 30H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.36 (d, *J* = 12.4 Hz, 1H), 4.1 – 4.2 (m, 6H), 3.5 – 4.1 (m, 35H), 3.44 (m, 1H), 3.28 (m, 1H), 3.17 (t, *J* = 6.9 Hz, 2H), 2.34 (s, broad, 3H, OH), 1.5 (m, 4H), 1.28 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8, 138.7, 138.6 (24 carbons), 138.5 (2 carbons), 138.4, 138.37 (4 carbons), 138.2 (2 carbons), 138.1, 138.0 (2 carbons), 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 101.7, 101.3, 101.0, 99.8, 97.0, 96.9, 80.2, 80.0, 79.7, 78.0, 77.9, 77.4, 75.2 (2 carbons), 75.1 (4 carbons), 74.9 (3 carbons), 74.3 (2carbons), 74.2, 73.6, 73.5 (2 carbons), 73.4, 73.2, 72.7, 72.37, 72.30, 72.2 (2 carbons), 72.0 (5 carbons), 71.7 (3 carbons), 71.5 (2 carbons), 71.3, 69.7, 69.2, 68.9 (2 carbons), 68.8 (2 carbons), 68.6 (2 carbons), 68.5, 68.0 (2 carbons), 67.6, 66.0, 65.7, 51.4, 29.3 28.8, 26.6, 25.8; ESI/APCI Calcd for $C_{154}H_{169}N_3O_{31}Na$ ($[M+Na]^+$) m/z 2579.1632; measured m/z 2579.1593.

6′-Azidohexyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (129). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.47 (t, *J* = 9.6 Hz, 1H, H-4), 4.97 – 5.3 (m, 3H), 4.84 (dd, *J* = 3.8, 10.3 Hz, 1H), 4.46 (d, *J* = 6.8 hz, 1H), 4.0 – 4.3 (m, 4H), 3.87 9m, 1H), 3.68 (m, 2H), 3.43 (m, 2H), 3.27 (t, *J* = 6.9 Hz, 4H)2.0 – 2.2 (m, 20H), 1.69 9m, 6H), 1.38 (m, 6H); ESI/APCI Calcd for $C_{20}H_{35}N_4O_{10}$ ($[M+NH_4]^+$) m/z 491.2353; measured m/z 491.2345.

6′-Azidohexyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (130).[78] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.0 – 5.5 (m, 4H), 5.00 (dd, *J* = 3.4, 10.3 Hz, 1H), 4.44 (d, *J* = 7.9 Hz, 1H), 4.1 (m, 4H), 3.89 (m, 2H), 3.67 (m, 1H), 3.43 (m, 2H), 3.26 (t, *J* = 6.9 Hz, 4H),

2.14 (s, 6H, 2 CH_3), 2.06 (s, 3H, CH_3), 2.04 (s, 6H, 2 CH_3), 1.98 (6H, 2 CH_3), 1.60 (m, 4H0, 1.38 (m, 4H).

6′-Azidohexyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside (131). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.49 (t, *J* = 9.7 Hz, 1H), 5.16 (t, *J* = 9.8 Hz), 5.00 (d, *J* = 3.5 Hz, 1H), 4.95 (m, 3H), 4.80 (dd, *J* = 3.6, 10.2 Hz, 1H), 4.46 (d, *J* = 6.8 Hz), 3.79 (dd, *J* = 5.9, 10.8 Hz, 2H), 3.70 (m, 2H), 3.61 (t, *J* = 2.9 Hz, 2H), 3.4 (m, 2H), 3.27 (t, *J* = 6.9 Hz, 4H), 2.07 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.05 (s, 3H), 2.04 (s, 3H, CH_3), 1.60 (m, 4H), 1.4 (m, 4H); ESI/APCI Calcd for $C_{17}H_{31}N_4O_8$ ($[M+NH_4]^+$) m/z 419.2141; measured m/z 419.2139.

6′-Azidohexyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranoside (132).[78] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.30 (d, *J* = 3.5, 10.0 Hz, 1H), 5.22 (dd, *J* = 1.7, 3.4 Hz, 1H), 5.07 (t, *J* = 9.9 Hz, 1H), 4.70 (d, *J* = 1.6 Hz, 1H), 3.8 (m, 1H), 3.67 (m, 1H), 3.4 (m, 1H), 3.28 (t, *J* = 6.9 Hz, 2H), 2.15 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 1.99 (s, 3H, CH_3), 1.6 (m, 4H), 1.4 (m, 4H), 1.22 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 170.2 (2 carbons), 97.7, 71.4, 70.2, 69.4, 68.2, 66.5, 51.6, 29.4, 28.9, 25.9, 21.1, 20.9, 20.9, 17.6.

6′-Azidohexyl 2,3,4-tri-*O*-acetyl-α-L-fucopyranoside (133). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.58 (dd, *J* = 3.4, 9.7 Hz, 1H), 5.32 (dd, *J* = 1.1, 3.3 Hz, 1H), 5.15 (dd, *J* = 3.7, 10.7 Hz, 1H), 5.08 (d, *J* = 3.7 Hz, 1H), 4.18 (m, 1H), 3.64 (m, 1H), 3.4 (m, 1H), 3.23 (t, *J* = 6.9 Hz, 2H), 2.20 (s, 3H), 2.14 (s, 3H), 2.02 (s, 3H), 1.6 (m, 4H), 1.4 (m, 4H), 1.16 (d, *J* = 5.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9, 170.7, 170.3, 96.3, 71.4, 68.6, 68.3, 64.5, 51.6, 29.9, 29.4, 29.0, 26.7, 25.9, 21.0, 20.9, 20.8, 16.1; ESI/APCI Calcd for $C_{18}H_{33}N_4O_8$ ($[M+Na]^+$) m/z 433.2298; measured m/z 433.2313.

6′-Azidohexyl 2,3,4-tri-*O*-acetyl-β-L-fucopyranoside (134).[78] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.23 (d, *J* = 3.4 Hz, 1H), 5.20 (dd, *J* = 7.9, 10.4 Hz, 1H), 5.02 (dd, *J* = 3.4, 6.9 Hz, 1H), 4.40 (d, *J* = 7.9 Hz, 1H), 3.9 (m, 1H), 3.77 (m, 1H), 3.45 (m, 1H), 3.26 (t, *J* = 6.9 Hz, 2H), 2.16 (s, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 1.61 (m, 4H), 1.38 (m, 4H), 1.25 (d, *J* = 6.4 Hz, 3H, CH_3).

6′-Azidohexyl 2,3,4-tri-*O*-acetyl-β-D-maltopyranoside (135). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.48 (m, 1H), 5.3 (m, 3H), 5.2 (m, 2H), 5.1 (m, 4H), 4.9 (m, 5H), 4.85 (m, 1H), 4.78 (m, 1H), 4.46 (m, 4H), 4.0 – 4.2 (m, 6H), 3.89 (m, 1H), 3.65 (m, 1H), 3.38 (t, *J* = 6.9 Hz, 2H), 3.26 (t, *J* = 6.9 Hz, 2H), 1.97 – 2.2 (m), 1.6 (m, 8H), 1.4 (m, 8H); ESI/APCI Calcd for $C_{32}H_{51}N_4O_{18}$ ($[M+NH_4]^+$) m/z 779.3198; measured m/z 779.3206.

6′-Azidohexyl 2-*O*-(2-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (136). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.2 – 7.4 (m, 45H), 5.17 (s, 1H), 5.15(d, *J* = 1.7 Hz, 1H), 4.8 – 4.9 (m, 3H), 4.5 – 4.7 (m, 15H), 4.23 (s, 2H), 4.12 (s, 1H), 3.86 – 4.0 (m, 7H), 3.65 – 3.84 (m, 9H), 3.5 (m, 1H), 3.27 (m, 1H), 3.22 (t, *J* = 6.9 Hz, 2H), 1.7 (s, 3H, CH3), 1.55 (m, 4H), 1.31 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 138.8, 138.7, 138.6 (2 carbons), 138.57 (2 carbons), 138.5 (2 carbons), 138.4, 128.7 (2 carbons), 128.6 (5 carbons), 128.5 (5 carbons), 128.4 (4 carbons), 128.3 (2 carbons), 128.2 (3 carbons), 128.1 (5 carbons), 128.0 (4 carbons), 127.95 (5 carbons), 127.90 (5 carbons), 127.7 (5 carbons), 100.9, 99.4, 98.9, 79.8, 75.5, 75.4 (3 carbons), 75.2 (2 carbons), 75. (2 carbons), 74.9, 74.6, 73.5 (4 carbons), 72.7, 72.5 (2 carbons), 72.3, 72.29 (2 carbons),

72.0, 70.8, 69.5, 67.7, 51.6, 29.5, 28.9, 26.7, 25.9, 21.1; ESI/APCI Calcd for $C_{89}H_{99}N_3O_{17}Na$ ($[M+Na]^+$) m/z 1504.6872; measured m/z 1504.6895.

6′-Azidohexyl 6-*O*-(2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-2-*O*-(2,6-di-*O*-acetyl-3,4-di-*O*-benzyl-α-D-mannopyranosyl)-3,4-di-*O*-benzyl-α-D-mannopyranoside (137). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.2 – 7.4 (m, 30H), 5.59 (s, 1H), 5.43 (s, 1H), 5.08 (s, 1H), 4.9 (m, 4H), 4.7 (m, 5H), 4.45 – 4.6 (m, 5H), 4.3 (m, 4H), 3.9 – 4.1 (m, 5H), 3.7 (m, 5H), 3.63 (m, 2H), 3.37 (m, 1H), 3.25 (t, *J* = 6.9 Hz, 2H), 2.13 (s, 6H), 2.05 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.57 (m, 4H), 1.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.9 (2 carbons), 170.2, 170.17, 138.3 (2 carbons), 138.26, 138.2, 138.0, 137.8, 128.6 (5 carbons), 128.4 (5 carbons), 128.3 (3 carbons), 128.2 (3 carbons), 128.1 (5 carbons), 128.0 (5 carbons), 127.9 (2 carbons), 127.7 (2 carbons), 99.7, 98.7, 97.6, 80.1, 78.3, 78.2, 75.3 (5 carbons), 74.9, 74.8, 74.2, 74.1,72.3, 72.1, 71.8, 70.4, 69.9, 68.6, 68.4, 67.7, 66.8, 51.5, 29.5, 28.9, 26.8, 26.1, 21.2 (2 carbons), 21.0 (2 carbons); ESI/APCI Calcd for $C_{74}H_{87}N_3O_{20}Na$($[M+Na]^+$) m/z 1360.5781; measured m/z 1360.5790.

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APPENDIX